ARCHIVES OF OPHTHALMOLOGY

VOLUME 38 (old series Volume 95) AUGUST 1947 NUMBER 2

COPYRIGHT, 1947, BY THE AMERICAN MEDICAL ASSOCIATION

# AUTONOMIC NERVOUS SYSTEM AND ACTION OF DRUGS IMPORTANT IN OPHTHALMOLOGY

H. B. VAN DYKE, M.D.
NEW YORK

THE IMPORTANCE of the autonomic nervous system needs little emphasis. It regulates the essential involuntary activities of the body. These include such varied functions as respiration, the circulation of the blood, digestion, metabolism, heat regulation and control of glands of internal secretions so far as these are under nervous control. If the acetylcholine theory of neuromyal transmission is completely adopted, even the voluntary musculature can be considered closely related to the autonomic nervous system. For an understanding of the pharmacology of autonomic drugs important in ophthalmology, it seems desirable to include a discussion of the general pharmacology of the whole autonomic system, in or from which, according to modern theory, nerve impulses are transmitted by a humoral mechanism. The transmitting substances are believed to be acetylcholine (synaptic transmission in the central nervous system [?] and in all autonomic ganglions; neuromyal transmission in striated muscle; transmission from postganglionic parasympathetic fibers to effector cells) and epinephrine or the closely related sympathins (transmission from postganglionic sympathetic fibers to effector cells).

Recently, the concept of cholinergic neurohumoral transmission has been questioned by Nachmansohn,[1] who expressed the belief that acetylcholine is concerned only in conduction. He remarked:

> . . . Cole and Curtis have shown by alternating current impedance measurements that the action potential is associated with a transient change in resistance which falls from 1000 ohm per cm $^2$ to 25 ohm. It is conceivable that a substance which appears and disappears within milliseconds could be responsible for these changes. The depolarization may be caused by the release of ACh at the point where the stimulus reaches the surface of the membrane. Thus, flow of current is generated to this point from the adjacent regions. This flow of current acts as stimulus of the next section and releases ACh there. The same process is repeated and thus the impulse is conducted along the fiber. This idea is quite compatible with the concept of propagated impulses as developed by Keith Lucas and Adrian. The

From the Department of Pharmacology, Columbia University College of Physicians and Surgeons.

1. Nachmansohn, D.: The Role of Acetylcholine in the Mechanism of Nerve Activity, in Harris, R. S., and Thimann, K. V.: Vitamins and Hormones, New York, Academic Press, Inc., 1945, vol. 3, pp. 337-377.

polarized state is rapidly restored by the removal of the free ester by its hydrolysis. At the nerve ending where the surface increases and therefore the resistance decreases this process would lead to a greater flow of current, thus enabling the impulse to cross the non-conducting gap.

In the original theory, ACh liberated at the nerve ending acts as "humoral" or "neurohumoral" transmitter directly on the effector organ or on the second neuron. According to the new concept, the release of ACh is an intracellular process generating flow of current by action on the cell membrane, but the transmitting agent is the flow of current. As outlined above, the electrical signs of nerve activity do not justify the assumption of a special mechanism responsible for transmission at synapses.

One frequently cited objection to Nachmansohn's theory is the failure to implicate acetylcholine in conduction along sensory nerves or sympathetic nerves. An even more serious discrepancy is the failure of antiesterases to alter conduction, as reported by Crescitelli, Koelle and Gilman.[2] These authors found that complete destruction of cholinesterase by diisopropyl fluorophosphate failed to interfere with nerve conduction. Yet such interference should be found according to Nachmansohn's theory, since conduction should be associated with extremely rapid destruction of the transiently formed acetylcholine. Rothenberg and Nachmansohn [3] disagreed with the conclusions of Crescitelli, Koelle and Gilman.

Eccles [4] proposed an alternative electrical hypothesis to explain synaptic and neuromuscular transmission but admitted that this hypothesis "will have to stand up to many severe tests, particularly pharmacologically."

For the purposes of this discussion, the older view that transmission of impulses depends on humoral agents, such as acetylcholine and substances closely related to epinephrine, will be adopted, since such a systematic approach is supported by a large body of experimental data and a consistent picture of the mechanism of action of drugs affecting the autonomic nervous system can be drawn. However, in view of recently expressed opinions to the contrary, the reader should recognize the biased approch adopted by the reviewer.

## GENERAL ANATOMY AND PHARMACOLOGY OF THE AUTONOMIC NERVOUS SYSTEM

Anatomically, the various divisions of the autonomic nervous system proper consist of three main divisions. The afferent portion consists of

2. Crescitelli, F.; Koelle, G. B., and Gilman, A.: Nerve Conduction in the Absence of Cholinesterase Activity Induced by Di-Isopropyl Fluorophosphate, Federation Proc. **5**:172, 1946.

3. Rothenberg, M. A., and Nachmansohn, D.: On the Permeability of the Nerve Axon to Di-Isopropylfluorophosphate, Federation Proc. **5**:199-200, 1946.

4. Eccles, J. C.: An Electrical Hypothesis of Synaptic and Neuromuscular Transmission, Nature, London **156**:680-683, 1945.

medullated fibers, which may make up a large proportion of a given autonomic nerve. Unfortunately, information on the importance of these afferent fibers—however great that importance may be—is restricted. In the central nervous system there are integrating structures at all levels, not only in the spinal cord but also in the medulla, in the midbrain and hypothalamus and in the cerebral cortex. The third, or efferent, division is the one most accessible for investigation. It is natural, therefore, that the most precise information concerns the distribution and functions of this portion. In the efferent autonomic nervous system, there is one ganglionic synapse between the central nervous system and the effector cell. Unlike the cells of the skeletal musculature, these effector cells can still function fairly adequately after the postganglionic fiber has been severed, although the disturbance which occurs after denervation is more pronounced in the parasympathetic division than in the sympathetic division, owing to the greater importance of the former. It is also characteristic of denervated autonomically innervated structures that their susceptibility to drugs may be markedly increased.

Some generalizations can be made concerning anatomic and physiologic differences between sympathetic and parasympathetic efferent divisions. The intervening ganglion cell is often close to the viscus on the parasympathetic side, whereas on the sympathetic side the intervening ganglion cell is far from the viscus. A single axon entering a sympathetic ganglion may transmit impulses to a number of ganglionic neurons, whereas in parasympathetic ganglions each neuron more often receives the transmitted nerve impulse from a single axon. Hence the response of the sympathetic system tends to be diffuse, in contrast with the more localized and precise response of the parasympathetic nervous system. It is also well to remember that the question of innervation of the cells of a single structure supplied by the sympathetic and the parasympathetic fibers is not clear. It appears likely that no single cell has a dual innervation. The number of fibers supplying a given effector cell varies greatly. For example, smooth muscle cells may receive fibers only occasionally, whereas each cell of the ciliary muscle has its individual nerve supply.

No effort will be made to describe in any detail the anatomic divisions of the autonomic nervous system. It will be recalled that the sympathetic nerves arise from the intermediolateral region of the gray matter of the spinal cord from the seventh cervical segment to the third lumbar segment inclusive. The ganglions of the sympathetic system are of three types: the vertebral ganglions in the thoracic and lumbar regions, in close proximity to the spinal column; the large prevertebral ganglions, such as the celiac ganglion and the superior mesenteric gan-

glion (the inferior mesenteric ganglion is seen much more frequently in lower animals than in man), and, lastly, the visceral ganglions, sometimes lying in the wall of the viscus. The parasympathetic division is composed of nerves of cranial origin, as well as nerves derived from the second to the fourth sacral segment of the spinal cord. Four cranial nerves give off branches which are classified as parasympathetic: branches of the third nerve, arising in the midbrain; branches of the seventh nerve supplying the submaxillary gland, as the chorda tympani, and the lacrimal gland, as the vidian nerve; the branch of the ninth nerve passing to the otic ganglion and thence to the parotid gland, and the important vagus nerve, which innervates numerous viscera in the thorax and abdomen.

Excellent reviews of the experimental basis for the theory of neurohumoral transmission of nerve impulses are available, and one of the most recent, which is highly recommended to the ophthalmologist, is that of Loewi.[5] To the other pioneer investigator in this field, H. H. Dale, are owed the generally adopted adjectives adrenergic and cholinergic, to identify the transmitting substance as either epinephrine or acetylcholine without regard to strict anatomic origin.[6] (Particularly in the sympathetic division is there frequently cholinergic transmission.) It appears that epinephrine is the common agent transmitting sympathetic adrenergic impulses. However, Cannon and his collaborators expressed the belief that it (substance M) combines at the site of action with one of two other substances to form sympathin E or sympathin I, according to whether the response is excitation or inhibition.[7]

Adrenergic transmission is characteristic of all sympathetic postganglionic efferent sympathetic nerves except the following, in which the mechanism is cholinergic:

1. Vasodilator nerves (except those of the coronary arteries and part of the arterial supply of skeletal muscle)
2. Sympathetic nerves to the sweat glands
3. Sympathetic nerves to the adrenal medulla (These nerves should be classified as preganglionic fibers, since the chromaffin cells of the adrenal medulla are analogous to sympathetic ganglion cells elsewhere.)

Cholinergic transmission, which is here considered as neurohumoral transmission the humoral moiety of which is acetylcholine, is responsible for transmission in the following structures:

---

5. Loewi, O.: Aspects of the Transmission of the Nervous Impulse, J. Mt. Sinai Hosp. **12**:803-816 and 851-865, 1945.

6. Dale, H. H.: Nomenclature of Fibres in the Autonomic Nervous System and Their Effects, J. Physiol. **80**:10P-11P, 1934.

7. Cannon, W. B., and Rosenblueth, A.: Sympathin E and Sympathin I, Am. J. Physiol. **104**:557-574, 1933.

1. All synaptic transmission in autonomic ganglions (nicotinic effect of acetylcholine).
2. All transmission from the end plate of skeletal nerves to skeletal muscle (nicotinic effect).
3. Transmission from all parasympathetic postganglionic efferent fibers to the corresponding end organ (muscarinic effect).
4. Neurohumoral transmission by certain postganglionic efferent sympathetic nerves, such as vasodilator nerves and the nerves to sweat glands (muscarinic effect).

Much work has been undertaken to determine whether acetylcholine is concerned in synaptic transmission in the central nervous system. The available evidence so far does not permit any conclusion, although considerable data suggest that the central nervous system contains only true cholinesterase, so that it may be presumed that acetylcholine is formed in connection with central nervous activity and that the cholinesterase there present is available for its rapid hydrolysis.

It is likely that the transmitting agent, whether epinephrine or acetylcholine, exists in a bound, nondiffusible form, from which extremely rapid liberation occurs during nerve stimulation. The rapidity of release probably varies. For example, acetylcholine is much more rapidly released and destroyed in junctional transmission in synapses or in neuromyal transmission in skeletal muscle—both "nicotinic" in character —than in the "muscarinic" type of response evoked when postganglionic parasympathetic fibers are excited.

### ACTION OF AUTONOMIC DRUGS IMPORTANT IN OPHTHALMOLOGY

Some information concerning the formation and destruction of the transmitting agents is available. The findings are important for an understanding of the action of adrenergic drugs, like cocaine and possibly ephedrine and related compounds, as well as of cholinergic drugs, like physostigmine and neostigmine. For the purposes of this discussion, epinephrine will be considered the important agent for adrenergic transmission, although Cannon and his co-workers have concluded that the primary, or common, transmitting agent (substance M, or epinephrine) is further modified, depending on the response of the innervated structure. The principal enzymes which have been implicated in the destruction of epinephrine are amine oxidase and catechol (pyrocatechol) oxidase. Inhibition of the destructive action of amine oxidase appears best to explain the sympathomimetic action of cocaine, which is believed to compete with epinephrine as a substrate for amine oxidase. Thus, locally liberated epinephrine will not undergo its normal rapid destruction but will act long and persistently. This mechanism makes intelligible the mydriatic effect of cocaine, as well as its sensitizing or potentiating

action if epinephrine is applied locally or administered systemically after or with cocaine. Gaddum has strongly advocated the view that ephedrine behaves similarly and that part of its sympathomimetic action is thus to be explained. It is likewise possible that related compounds, such as amphetamine ("benzedrine") and desoxyephedrine in part owe their sympathomimetic effects to competitive binding of amine oxidase.

Epinephrine can be regarded as the truest sympathomimetic drug. It acts on the sympathetically innervated cell and evokes a response identical with that of electrical stimulation of sympathetic nerves. All the synthetic related compounds differ slightly or greatly from epinephrine either in potency or in qualitative action or in both. Those drugs which are also potentiated by cocaine, such as "arterenol" (3, 4-dihydroxyphenylaminoethanol) or "corbasil" (3, 4-dihydroxyphenylaminopropanol), probably resemble epinephrine most closely pharmacologically. According to available evidence, two sympathomimetic drugs used in ophthalmology, "neo-synephrine hydrochloride" and paredrine (p-hydroxy-*a*-methylphenylethylamine), are likewise best classified as sympathomimetic stimulating agents. Lastly, although it was suggested in the foregoing paragraph that ephedrine, amphetamine and desoxyephedrine may, like cocaine, inhibit the enzymic destruction of epinephrine, their action is not as clearly limited to this mechanism; in part, they probably directly stimulate some, but not all sympathetically innervated structures.

Much more accurate information is available concerning acetylcholine, the agent responsible for neurohumoral transmission in autonomic ganglions, from skeletal nerves to muscle and from postganglionic parasympathetic nerves to their end organs. Although drugs are not known to affect the formation of acetylcholine, it is of interest to record that Nachmansohn and Machado [8] have shown that an enzyme in the central nervous system which they named choline acetylase can bring about synthesis of this transmitting agent. There are required not only the enzyme but also choline, acetate, adenosine triphosphate and an optimum concentration of potassium. The enzymic acetylation of choline is an anaerobic process which so far has been shown to occur only in nerve tissue. Presumably after formation acetylcholine is bound in some nondiffusible form, from which it is liberated during nervous activity. In the scheme of acetylcholine formation just described an optimum concentration of potassium was mentioned. This cation is an important factor in nervous activity. Appropriate doses of potassium cause the liberation of acetylcholine from ganglion cells or of epinephrine from the adrenal glands. The cation, however, is not the mediator of adrenergic transmission, as has beeen maintained by some workers.

8. Nachmansohn, D., and Machado, A. L.: The Formation of Acetylcholine: A New Enzyme; Choline Acetylase, J. Neurophysiol. **6**:397-403, 1943.

More pertinent to this discussion is the manner in which certain drugs prevent the hydrolysis of acetylcholine. This destruction is ordinarily effected by cholinesterase, an enzyme found in nerve tissue and, paradoxically, also in erythrocytes. (There are also a number of nonspecific esterases in serum and tissues, which vary in the rate at which they hydrolyze acetylcholine.) Cholinesterase as well as nonspecific esterases are markedly inhibited both by physostigmine and by neostigmine. Carbaminoylcholine can also inhibit the action of cholinesterase. Of great interest is the destructive action of diisopropyl fluorophosphate (DFP) on cholinesterase, which apparently is irreversibly inactivated by this enzyme poison. The antiesterase effect of physostigmine, neostigmine and DFP explains the parasympathomimetic actions of these compounds, so that they are pharmacologically comparable to cocaine, which is a sympathomimetic agent by virtue of its inhibition of amine oxidase, an enzyme-destroying epinephrine.

The antiesterase effect of physostigmine, neostigmine and DFP permits locally formed acetylcholine to produce continuous and cumulative "stimulation" of the cells on which this transmitting agent acts. Although physostigmine and DFP would have no action were acetylcholine not liberated and of themselves cannot excite cells under the control of cholinergic nerves, it has recently been reported that neostigmine not only inactivates cholinesterase but also stimulates effector cells with a cholinergic innervation.[9] Riker and his colleagues also pointed out, as has already been mentioned, that carbaminoylcholine, particularly among synthetic choline esters, can inhibit cholinesterase. One of the most interesting antiesterases is diisopropyl fluorophosphate (DFP), which irreversibly destroys cholinesterase and other esterases. Its persistent and remarkable cholinergic effects in the normal or the glaucomatous human eye [10] are to be attributed to normally liberated acetylcholine, the action of which persists because the enzyme responsible for its hydrolysis has been destroyed.

Other parasympathomimetic drugs act only or principally as agents stimulating cells normally thus affected by impulses transmitted from postganglionic parasympathetic nerves. The normal transmitting agent, acetylcholine, is too rapidly hydrolyzed by the abundant amounts of cholinesterase and other esterases ordinarily present to be of any practical value as a parasympathomimetic drug. However, one of its congeners, carbaminoylcholine chloride ("carcholin") not only is not destroyed by cholinesterase but actually inhibits the enzyme. It is also probably a parasympathomimetic stimulant. Another synthetic relative of acetyl-

9. Riker, W. F.; Wescoe, W. C.; Cattell, McK., and Shorr, E.: The Mechanism of Action of Prostigmine, Federation Proc. **5**:198-199, 1946.

10. Leopold, I. H., and Comroe, J. H.: The Effects of Di-Isopropyl Fluorophosphate upon Normal and Glaucomatous Eyes, Federation Proc. **5**:190, 1946.

choline, acetyl-β-methylcholine ("mecholyl") is less readily hydrolyzed by cholinesterase than is acetylcholine. Acetyl-β-methylcholine is thus a more persistent parasympathomimetic agent than acetylcholine but cannot approach carbaminoylcholine in this respect. At least in the eye, pilocarpine behaves like acetylcholine and in exciting the circular smooth muscle of the ciliary body and the iris acts analogously to the normal neurohumoral transmitter.

The drugs which remain to be considered are those paralyzing effector cells innervated by postganglionic parasympathetic fibers. (Drugs like ergotoxine or ergotamine, having in part a similar action on sympathetically innervated structures, have little apparent value to the ophthalmologist.) The important group paralyzing the muscarinic effects of acetylcholine in the eye, comprising drugs like atropine, homatropine, eucatropine (euphthalmine), scopolamine and duboisine, vary in potency and persistence of action. They do not interfere with the liberation of acetylcholine, nor do they facilitate its hydrolysis; they act by denying acetylcholine or a drug like pilocarpine access to the irritable "patches" of effector cells, where it is believed the response of the cells begins. Perhaps a drug like atropine, one of the most persistent and active members of this group, combines more firmly and less reversibly with an important constituent of the irritable "patches" of cell surfaces than transiently acting drugs, like homatropine. The "patches" may thus be rendered incapable of combination with or response to either acetylcholine or pilocarpine. The antagonism of physostigmine by atropine or related drugs is in reality an antagonism of atropine toward acetylcholine protected from hydrolysis by physostigmine inhibition of cholinesterase. Some drugs, such as carbaminoylcholine are much less effectively counteracted by atropine. Homatropine and eucatropine (euphthalmine), as well as the less important other members of the group, resemble atropine pharmacologically, although there are quantitative differences in action. It is well known that the effects of homatropine are much less persistent and that eucatropine, while causing mydriasis, has little effect on accommodation.

## SUMMARY

The outline which follows is restricted to drugs which are used in ophthalmology or are believed to be potentially useful (e. g., DFP). Some which are included for completeness (e. g., scopolamine and duboisine) are considered by the reviewer to be superfluous except when drug idiosyncrasy is present. Inability to explain drug action rigidly is reflected in the duplicate classifications of ephedrine, amphetamine, neostigmine and "carcholine."

I. Drugs acting on the adrenergic postganglionic nerves of the sympathetic division

A. Enzyme-inhibitors preventing the destruction of epinephrine, which is essential for neurohumoral transmission in this division. The locally produced epinephrine thus has a prolonged effect.

1. Cocaine
2. Ephedrine (?)
3. Amphetamine ("benzedrine") (?)

B. Drugs acting on effector cells so as to mimic the action of the neurohumoral transmitter

1. Epinephrine ("adrenalin")
2. "Neo-synephrine hydrochloride"
3. Paredrine
4. Ephedrine
5. Amphetamine ("benzedrine")

II. Drugs acting on cholinergic postganglionic nerves, which in the eye are parasympathetic

A. Inhibitors of the enzyme cholinesterase, which normally hydrolyzes the neurohumoral transmitting agent acetylcholine. The action of the locally produced acetylcholine is therefore markedly prolonged

1. Physostigmine
2. Neostigmine
3. Diisopropyl fluorophosphate (DFP)
4. Carbaminoylcholine hydrochloride ("carcholine")

B. Drugs acting on effector cells so as to mimic the action of acetylcholine, the neurohumoral transmitter

1. Pilocarpine
2. Neostigmine (?)
3. Synthetic choline esters, such as carbaminolycholine

C. Drugs producing varying degrees of paralysis of effector cells to impulses from parasympathetic postganglionic nerves or to stimulation by drugs like pilocarpine. These paralyzing drugs prevent the access of acetylcholine or stimulating drug to the irritable patches of the surface of effector cells

1. Atropine
2. Homatropine
3. Eucatropine (euphthalmine)
4. Scopolamine
5. Duboisine

630 West One Hundred and Sixty-Eighth Street.

# SOFT GLAUCOMA AND CALCIFICATION OF THE INTERNAL CAROTID ARTERIES

JOHN M. McLEAN, M.D.
AND
BRONSON S. RAY, M.D.
NEW YORK

SINCE Fuchs's [1] paper in 1911, cases have been described with atrophy of the optic nerve, suggestive glaucomatous cupping and loss of visual field. The condition in these cases resembles chronic glaucoma but does not show elevation of intraocular pressure. It has been described by such terms as "soft glaucoma" and "glaucoma without hypertension."

In 1932 Knapp [2] reviewed the literature on this subject and described 10 cases of his own. All his cases were characterized by atrophy of the optic nerve with shallow cupping, defects of the visual fields which tended toward altitudinal hemianopsia and persistently normal tension. He was able to demonstrate roentgenographically calcification of the arteries at the base of the brain in all 10 cases. In 9 of these cases the internal carotid arteries were involved, either with or without involvement of other vessels in that region. He concluded that "the roentgen findings, not as yet confirmed by anatomic examination, suggest a possible cause." In 1940 Knapp [3] published a follow-up report on these cases. In most of them progress of the altitudinal field defects had been slow. Tension had remained normal or nearly normal. The loss in visual acuity and visual fields was out of proportion to the tension in the cases in which there had been slight elevations of intraocular pressure. In discussion of these cases, the rather common occurrence of calcification of the carotid artery in elderly persons with arteriosclerosis was noted and the incidence given as 1 in 8 persons [4]

---

From the Department of Surgery, the New York Hospital and Cornell University Medical College.

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, April 15, 1946.

1. Fuchs, E.: Ztschr. f. Augenh. **25**:108, 1911.

2. Knapp, A.: Association of Sclerosis of the Cerebral Basal Vessels with Optic Atrophy and Cupping, Arch. Ophth. **8**:637 (Nov.) 1932.

3. Knapp, A.: Course in Certain Cases of Atrophy of the Optic Nerve with Cupping and Low Tension, Arch. Ophth. **23**:41 (Jan.) 1940.

4. Glees, M., 1936, cited by Knapp.[3]

over the age of 50 and as 50 per cent of persons [5] over the age of 60. The suggestion is made [6] that damage to the optic nerve is caused by impairment of the small nutrient vessels of the nerve, rather than sclerosis and calcification of the carotid artery itself.

The case to be reported here belongs to this syndrome and is of interest because the mechanism of the disease process is demonstrated anatomically in the living patient.

## REPORT OF A CASE

M. S., a white man aged 61, had first noticed slight cloudiness of vision in 1935. At that time he consulted an ophthalmologist, who made a diagnosis of early glaucoma and prescribed pilocarpine. The next year he consulted another ophthalmologist, who assured him that he did not have glaucoma. In 1937 he

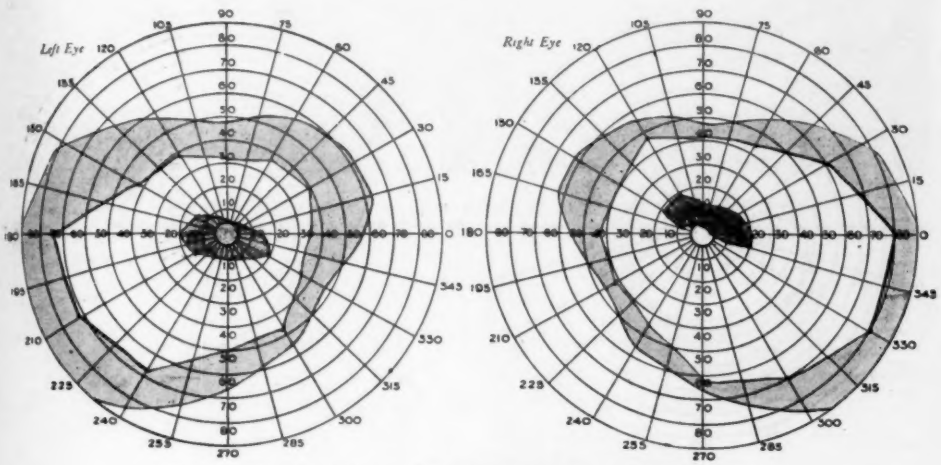



Fig. 1.—Visual fields in 1939 (courtesy of Dr. B. Samuels).

consulted several more ophthalmologists, from New York to California, and received varying opinions about the diagnosis of glaucoma. At no time was there any pain or redness of either eye or any iridescent vision. Tension had always been normal. Miotic therapy was continued. In 1939 an iridectomy was performed on the left eye by Dr. Bernard Samuels. Visual fields taken at that time are shown in figure 1. Corrected visual acuity was 20/20 in the right eye and 1/200 in the left eye. After operation the tension remained normal in both eyes with continued slow loss of visual acuity and visual field. In 1945 the patient consulted two other ophthalmologists in New York. One of them made a diagnosis of glaucoma on a "toxic" basis; the other, after extensive study and provocative tests, stated that there was no glaucoma. With this conflict in opinions, the patient consulted Dr. Alan Woods, of Baltimore, who found no evidence of glaucoma and referred him to us for study.

5. Siegert, P., 1938, cited by Knapp.[8]

6. Best, F., 1931, cited by Knapp.[8]

We first saw the patient on Dec. 5, 1945. On that date his corrected visual acuity was 20/70 in the right eye and 3/200 in the left eye. Except for an operative coloboma of the iris of the left eye, both eyes appeared normal for a person of his age on external examination. Tension was 22 mm. in the right eye and 18 mm. in the left eye with a McLean tonometer (lower range of normal). On ophthalmoscopic examination, the right optic disk showed moderate pallor with shallow, incomplete cupping, without undermining and not appearing of glaucomatous type. The left optic disk was extremely pale, with similar cupping. The retinal vessels showed only mild sclerotic changes. The fundi were otherwise not remarkable. Biomicroscopic examination disclosed gerontoxon; slight peripheral, superficial atrophy of the iris; early nuclear sclerosis of the lenses, more advanced on the left, and a cleancut coloboma of the iris of the left eye without synechias. There was no evidence of inflammatory disease. Gonioscopic examination revealed an essentially normal condition with only a few postoperative

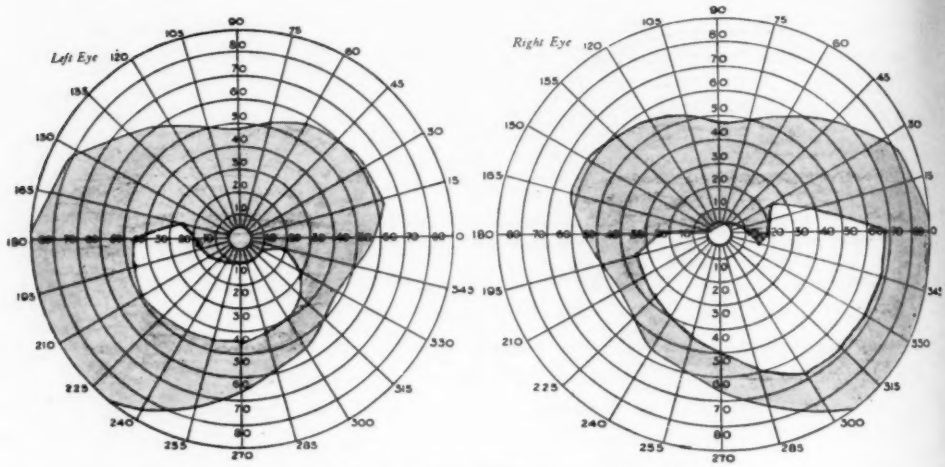



Fig. 2.—Visual fields at time of operation (1946).

adhesions in the angle of the left eye. The visual fields (fig. 2) showed extensive loss in the superior portion in each eye.

On Jan. 18, 1946, the patient was admitted to the New York Hospital for study. His medical history revealed that syphilis had been suspected in 1925 and an intensive course of arsenobismuth therapy given, apparently without definite proof of the disease. Frequent subsequent serologic tests had given negative reactions, and two examinations of the spinal fluid had revealed nothing abnormal. He had passed a small bladder stone in 1941. His medical history was otherwise essentially not remarkable. Physical examination (except for his eyes) showed only slight cardiac enlargement and a blood pressure of 155 systolic and 82 diastolic. The blood cells and urine were normal, and serologic tests for syphilis gave negative reactions. The electrocardiogram and the electroencephalogram were normal. Roentgenograms of the skull were normal and failed to disclose any unusual sclerosis of the carotid arteries (fig. 3). Lumbar puncture revealed that the spinal fluid was under normal pressure, with a normal protein content, a normal colloidal gold curve and a negative Wassermann reaction. Visual fields

as determined repeatedly were similar to those in figure 2. The water-drinking and homatropine provocative tests for glaucoma gave negative results. There seemed to be sufficient evidence of a lesion at the base of the brain to warrant exploration.

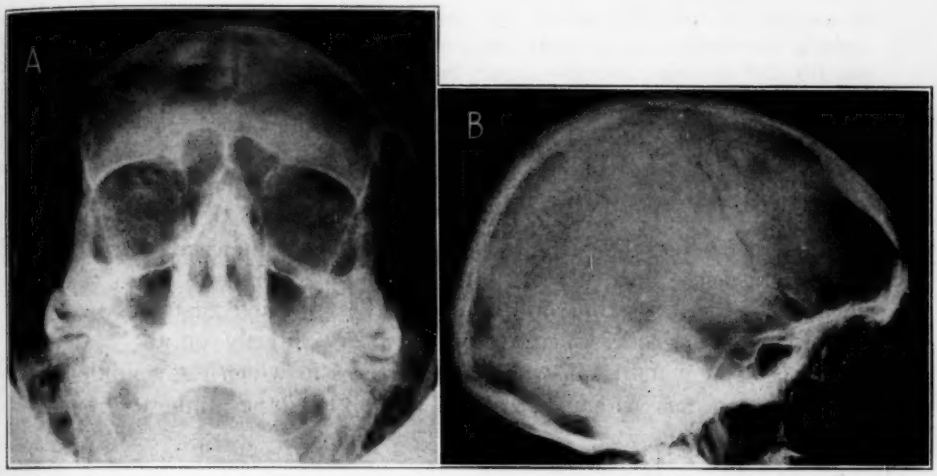



Fig. 3.—Roentgenograms of the skull.

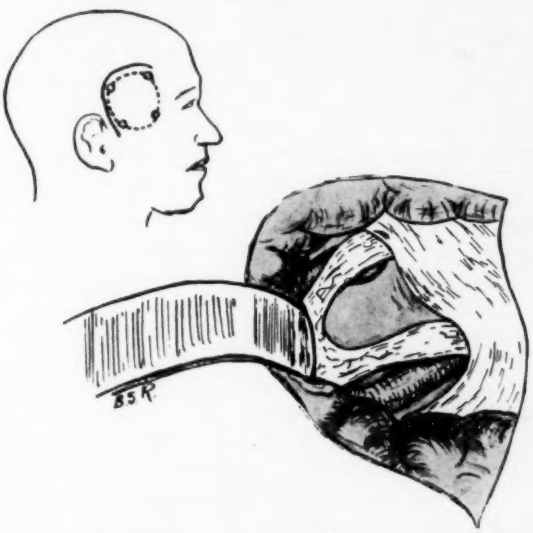


Fig. 4.—Sketch of exposure at operation.

Accordingly, on Jan. 28, 1946, one of us (B. R.) exposed the region of the chiasm and both optic nerves. This was done through an incision in the skin just behind the hair line and a frontotemporal bone flap. The frontal lobe was easily retracted, and the subarachnoid space was observed to be wide and free from

adhesions. There was no evidence of old or recent inflammatory disease or of neoplasm or aneurysm. The optic nerves were longer than usual and ran up over the internal carotid arteries. Both nerves appeared atrophic. At the point where the nerves crossed the arteries they were flattened in ribbon-like fashion. The internal carotid arteries beneath were sclerotic, and each had a calcified plaque in its wall directly under the nerve. On direct observation, these calcified plaques could be seen hammering against the optic nerves with each pulse beat (fig. 4). It was felt that nothing constructive could be done. The wounds were closed, and the patient had a satisfactory postoperative course. He made an uneventful recovery from the operation, with no postoperative change in visual acuity, visual fields and ophthalmoscopic appearance.

## CONCLUSION

This report presents definite evidence of the mechanism of injury to the optic nerve in a case of "soft glaucoma" accompanied with calcification of the internal carotid arteries. It is probable that pulsating pressure of a sclerotic, calcified carotid artery directly on the optic nerve may play a more important part in cases in which the condition simulates glaucoma without increased tension than has hitherto been supposed.

525 East Sixty-Eighth Street.

# CYCLOPEAN EYE AND LATERAL PROBOSCIS WITH NORMAL ONE-HALF FACE

## Report of a Case

LOUISE H. MEEKER, M.D.
AND
RUDOLF AEBLI, M.D.
NEW YORK

PRELIMINARY reports of this case were made in previous issues of the ARCHIVES.[1] At the time of its presentation the question was raised whether unilateral cyclopia, or three eyes in a single person, could be satisfactorily explained.

The literature contains many reports of cyclopean "monsters" but few cases of lateral proboscis, and these have excited less interest. We have not found described in the available literature a combination of these deformities and a normal one-half face, such as is present in our case.

The older authors, with rare exceptions, were content with anatomic descriptions of the malformations in their cases. As a rule, microscopic studies were not made, and the part played by heredity was ignored. Evolution from the blind belief in the supernatural to a scientific approach to these phenomena has been slow, owing partly to lack of data on family histories, except in a few cases. As certain types of malformations appeared frequently and experimental evidence was added, the individual cases were studied in greater detail with regard to possible causal factors. Harvey,[2] in 1651, attributed all congenital defects to phylogenetic processes. Sömmerring[3] (1791) and Stockard[4] stated

From the Department of Ophthalmology, Rudolf Aebli, M.D., Director, and the Department of Pathology, Maurice Richter, M.D., Director, of the New York Post-Graduate Medical School and Hospital and Columbia University.

1. The case was presented at meetings of the Section of Ophthalmology, New York Academy of Medicine, on April 21, 1941 and Feb. 21, 1944 (Lateral Proboscis with Demicyclopia, Arch. Ophth. **27**:623 [March] 1942; Lateral Proboscis with Cyclopean Eye, ibid. **31**:356 [April] 1944).

2. Harvey, W.: Anatomical Exercitations Concerning the Generation of Living Creatures, London, J. Young, 1653.

3. Sömmerring S. T.: Abbildungen und Beschreibungen einiger Misgeburten, Mainz, 1791.

4. Stockard, C. R.: The Development of Artificially Produced Cyclopean Fish—"The Magnesium Embryo," J. Exper. Zool. **6**:285, 1909.

that the type of deformity depends on the stage of embryonic development in which it occurs. This idea was linked to heredity by Meckel [5] in 1812. In 1882 His [6] expressed the belief that all malformations are related to a germinal defect. This opinion was amplified by Wilder [7] in 1908 and was further upheld by Fischel's [8] experiments (1921).

No attempt is made to review the older literature on cyclopia, as this has been done by Hill [9] (1920 and 1921), Chapman [10] (1936) and Wilbur [11] (1939). It is common to find certain other abnormalities associated with cyclopia, such as deformity of the palate, coloboma and other defects of the eyes, brain and skull, or a proboscis, usually situated above the central, cyclopean, eye. Less frequently, cleft palate and cleft lip are seen, and rarely polydactyly is present. Lateral proboscis is also frequently associated with cleft palate and coloboma of the eyelids.

It is of considerable interest that atypical monozygotic twinning sometimes occurs in cases of cyclopia and of lateral proboscis associated with coloboma. In relation to our case, the importance of twinning lies in the fact that incomplete separation of twins derived from a single ovum results in the formation of "monsters" of various types. When the separation is nearly complete, the result is the well known "Siamese twins." With further separation there may be duplication of only certain parts, such as the head or the facial features.

It is commonly accepted that cyclopean eye is one of the results of incomplete separation. Lateral proboscis has not previously been considered a result of atypical monozygotic twinning.

Modern studies include histologic details and results of experimental work. The influence of embryonic environment on the germ potentialities is also stressed. Our case represents a combination of defects of the eye and nose and closely related malformations of the face, which we shall consider in the light of present knowledge and attempt to formulate an interpretation.

---

5. Meckel, J. F.: Handbuch der pathologischen Anatomie, Leipzig, C. H. Reclam, 1812-1816.

6. His, W.: Anatomie menschlicher Embryonen: II. Gestalt- und Grössenentwicklung bis zum Schluss des 2 Monats, Leipzig, F. C. W. Vogel, 1882.

7. Wilder, H. H.: The Morphology of Cosmobia: Speculations Concerning the Significance of Certain Types of Monsters, Am. J. Anat. **8**:355, 1908.

8. Fischel, A.: Ueber die normale und abnorme Entwicklung des Auges, Arch. f. Entwcklngsmechn. d. Organ. **49**:383, 1921.

9. Hill, E.: Cyclopia: Its Bearing upon Certain Problems of Teratogenesis and of Normal Embryology with a Description of a Cyclocephalic Monster, Arch. Ophth. **49**:597, 1920; **50**:52, 1921.

10. Chapman, K. H.: Human Cyclopia, Arch. Ophth. **16**:40 (July) 1936.

11. Wilbur, I. E.: Human Cyclopia with Associated Ocular Anomalies: A Case Report and Embryological Interpretations, Am. J. Ophth. **22**:1120, 1939.

Fig. 1.—Kodachromes. *A*, 10 day infant with lateral proboscis, cyclopean eye and double corneas with two irises and two pupils. *B*, appearance seven months after removal of the proboscis, amputation of the anterior half of the globe and plastic closure of the socket. *C*, infant when 13 months old, showing flattening of the left side of the face and the forehead. The right side is normal, with normal eye and naris. The brown pigmentation on the skin is from eating chocolate. *D*, infant when 2 years old, showing flattening and underdevelopment of the left side of the face with the anterior portion of the cranium more pronounced than the rest of the skull. There is probable agenesis of the left cerebral hemisphere, with weakness of the right hand and foot. In mental status the child was at the moron level, with good behavior adjustment.

In a thorough search of the available literature, we have found no exact duplicate of the malformations present in our case. Therefore, we shall attempt here to discover its place in the graded types of malformations of the eye and nose delineated by Förster,[12] Sömmerring,[8] Wilder,[7] Rating [13] and Redenz.[14]

## REPORT OF CASE

*History.*—A 10 day old male infant was admitted to the service of Dr. Adolph De Sanctis at the New York Post-Graduate Medical School and Hospital on Sept. 30, 1940. He was the second child of normal parents, a full term 9 month infant, weighing 7 pounds 8 ounces (3,400 Gm.) at birth. Labor was normal. The child was well developed and of normal size; the abnormalities were confined to the head. The family history revealed nothing of significance except that the maternal grandfather was one of identical twins.

The left eye was greatly enlarged and proptosed (fig. 1 *A*), the conjunctiva was intensely chemotic and bulging, and a double cornea with two irises and two pupils was plainly visible. The nasal cornea showed necrosis, and the anterior chamber was cloudy, with hypopyon. The temporal cornea was clear, as was the anterior chamber beneath. The iris was a clear blue. Attached to the superior nasal part of the orbit, and freely movable, was a firm tubular structure 40 mm. long and about 10 mm. in diameter. An opening 2 mm. in diameter, through which mucus could be expressed, was present at the tip of this tubular structure. The right half of the nose and the right eye presented no abnormalities. Just above the upper lip in the midline there was a small protruding mass, which measured 0.5 by 0.5 cm. and was red and soft. On each side of the hard palate anteriorily there was a whitened area, about 1 by ½ inch (2.5 by 1.3 cm.) and not raised. A roentgenogram of the mouth showed developmental asymmetry and cleft hard palate. The skull was elongated in its vertical diameter, with wide spacing of the orbits and broadening of the nares; convolutional markings were accentuated, the parieto-occipital area and the sella turcica were about 20 per cent undersize.

The diagnosis was that of relatively small, underdeveloped left orbit and bones of the left side of the face, complete blockage of the left nasal region and underdeveloped sinuses.

In view of the presence of panophthalmitis, and in the absence of complete knowledge of what defects there might be in the bony structures behind the proptosed globe, removal of the anterior half of the globe with evisceration of the posterior contents of the eyeball seemed the procedure of choice. The idea of obtaining the eye in toto was reluctantly abandoned because of its purulent condition and the attendant hazard of death from meningitis.

On Oct. 3, 1940, with the patient under ether anesthesia induced by the drop method, the conjunctiva was cut around the limbus and freely undermined. The sclera was cut in a circular fashion about 6 mm. from the limbus, and the anterior

12. Förster, A. J. T.: Die Missbildung des Menschen systematisch dargestellt, Jena, F. Mauke, 1861.

13. Rating, B.: Ueber eine ungewöhnliche Gesichtsmissbildung bei Anencephalie, Virchows Arch. f. path. Anat. **288**:223, 1933.

14. Redenz, E.: Ueber Erscheinungsformen und Genese der Arhinenzephalie und Zyklopie und die Bedeutung gekoppelter Missbildungen, Ztschr. f. Geburtsh. u. Gynäk. **114**:185, 1937.

segment of the eyeball was removed. The posterior scleral cavity was eviscerated; apparently, only one cavity was present. The scleral sac was packed with iodoform gauze and the conjunctiva closed with interrupted silk sutures, leaving a small central opening for removal of the packing. The infant had an uneventful postoperative recovery, took his formula well and began to gain weight.

On December 12, with the infant under ether anesthesia, induced by the open drop method, the proboscis, in the nasal part of the left orbit, was removed and a plastic orbital reconstruction performed. The anomalous proboscis was raised, and on the nasal side a rectangular skin flap was fashioned. The proboscis was dissected down to its dense fibrous attachment to the superior nasal part of the

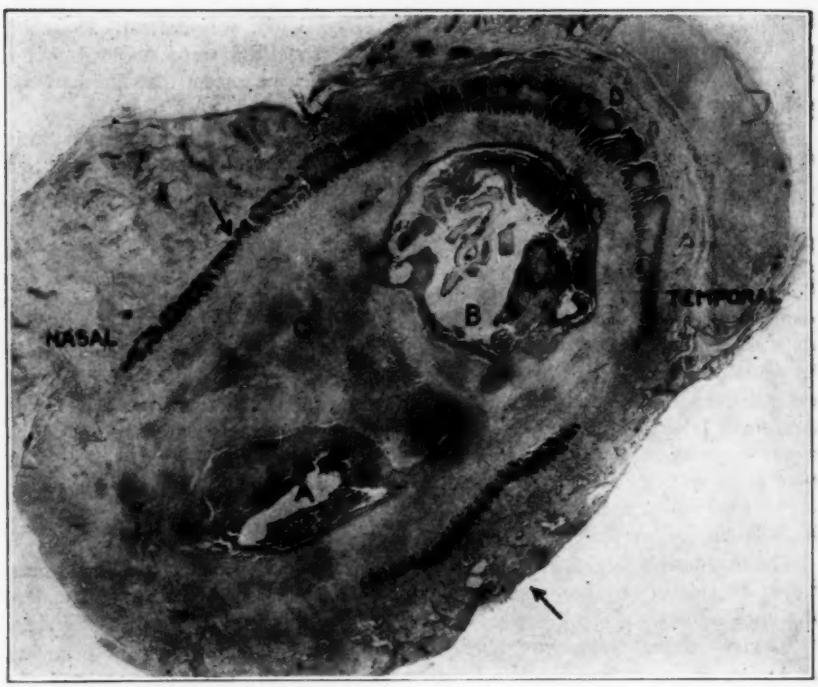



Fig. 2.—Microscopic section (oblique) from a cyclopean eye through the base of the cornea, measuring 16 by 8 mm. *A* and *B*, anterior chambers of the double cyclopean eye, with ulceration of the corneas. *C*, ciliary muscle (arrow marks the sclera). Purulent exudate is present in both *A* and *B*. *D*, corneal epithelium.

left orbit and was cut at its attachment. The short, tense left upper lid was cut parallel to the orbital ridge and split into two layers. The left lower lid was also split along the intermarginal white line into its two layers. The conjunctival layer of the freed upper lid and that of the lower lid were sutured together with chromic surgical gut. The cilia were excised from the outer layers, and the skin of the upper lid and that of the lower lid were sutured together with interrupted silk sutures. The rectangular pedicle skin flap, previously fashioned, was then trimmed and the defect in the upper lid closed with this skin flap. Postoperative healing was uneventful (fig. 1 *B*).

PATHOLOGIC EXAMINATION

*Eye.*—Gross Observations: The specimen from the eye was an oval disk of semitransparent fibrous tissue, 18 by 15 mm. in area and 2 mm. thick. The slightly convex surface showed wrinkled, white and gray tissue with two lateral, similarly depressed areas, a few millimeters in diameter, situated in the center of each half; these areas were partly necrotic and mottled with brown pigment. The under surface was lined with a ragged brown layer, suggesting iris, and flecks of pus clung to the irregular tabs.

Microscopic Observations: The specimen was embedded *in toto* in paraffin, and serial sections of the whole specimen were cut approximately in a frontal plane

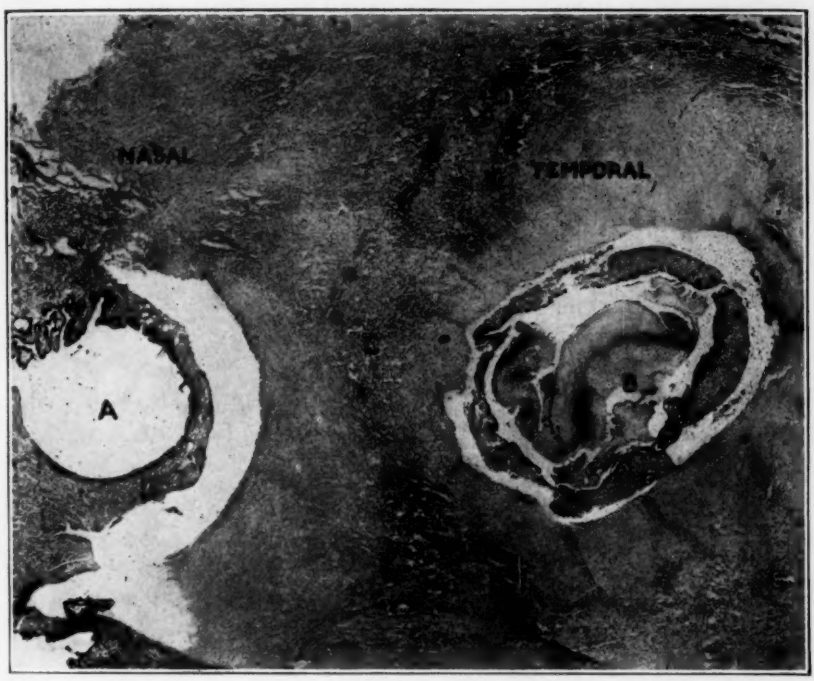



Fig. 3.—Microscopic section (oblique) through the ciliary region of the double cyclopean eye. *A*, one anterior chamber with iris and ciliary processes; *B*, anterior chamber, iris and prolapsed lens with colonies of bacteria; *C*, ciliary muscle and vessels of the anterior portion of the sclera.

and stained with hematoxylin and eosin. Interpretation was difficult because of the ulceration and the presence of purulent exudate and colonies of Staphylococcus aureus. The first sections showed two ulcerating areas in the cornea, with loss of tissue and two separate openings, the spaces extending completely through the cornea (fig. 2, *A* and *B*). A transversely elongated rim of stratified squamous epithelium with blunted rete pegs enclosed both spaces in a continuous layer, but they were separated by sclera (*C*) and ciliary muscle. Each opening (fig. 3, *A* and *B*) showed a pupil with an enclosing ring of iris and ciliary processes. The separate pupils were without pupillary membranes (fig. 5, ciliary epithelium in fig. 3, *B*).

*Nose.*—Gross Observations: The proboscis, on the left side, measured 4 cm. in length and 12 mm. in diameter at the tip and narrowed to 9 mm. at the root. It was covered with skin except at the line of excision. A canal, approximately 3 mm. in diameter, ran the entire length of the proboscis.

Microscopic Observations: Sections were made through the nostril, the mid-portion and the root of the nasal proboscis. Each area was lined with its normal mucous membrane. The nostrils were lined with squamous epithelium, hair and sebaceous glands (fig. 6). Normal schneiderian membrane, including mucous glands, covered the turbinate processes (fig. 7), with a thinner layer in the frontal

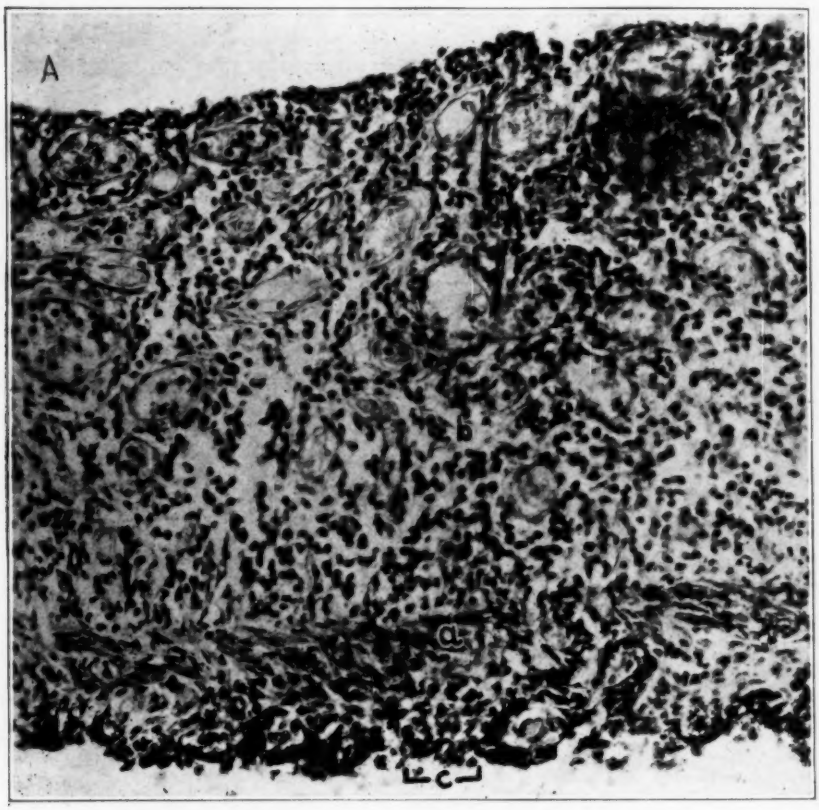



Fig. 4.—Microscopic section of the iris. *A* and *B* (from *A* and *B*, respectively, of figure 3): *a*, sphincter muscle of the iris; *b*, stroma, and *c*, pigment epithelium.

region of attachment (fig. 8). The plaques of cartilage were of fetal type but were found in the nares and the turbinate bone, and ossification was present at the root of the proboscis.

*Diagnosis.*—The diagnosis was cyclopean eye, double, and lateral proboscis, each on the left side.

*Course.*—During the succeeding three and one-half years the child was kept under observation and readmitted to the hospital at intervals for further study. At 7 months of age flattening of the left side of the face and of the forehead

was visible. The head was definitely misshapen, the entire right side being larger than the left (fig. 1 *C*). Roentgenograms of the skull and sinuses showed a small, underdeveloped left orbit and underdevelopment of the bones of the left side of face, complete blockage of the left nasal region and underdeveloped sinuses.

At 2 years of age (fig. 1 *D*) the flattening and underdevelopment of the left side of the face and the anterior portion of the cranium were more pronounced. Further roentgenographic study showed an evident congenital anomaly with

Figure 4 B

developmental asymmetry, there being a relatively small orbit on the left side, with bony condensation and hyperostosis of the left ethmoidal region and naris and wide spacing between the orbital margins. The antrums were poorly developed and the left naris was occluded. The hard palate was cleft and conically arched toward the left orbit, and the upper lip showed a streaked dimpling to the left of the columella. Neurologic examination showed reduction of the deep reflexes, weakness of the right hand and foot and probably agenesis of the left cerebral

hemisphere. Examination of the mental status indicated that intelligence was at the moron level, with good behavior adjustment.

At 3 years of age the abnormalities noted were more pronounced, and definite weakness of the right side was evident. The boy could now walk and play with his brother and say a few words, but his mental status was definitely on the moron level.

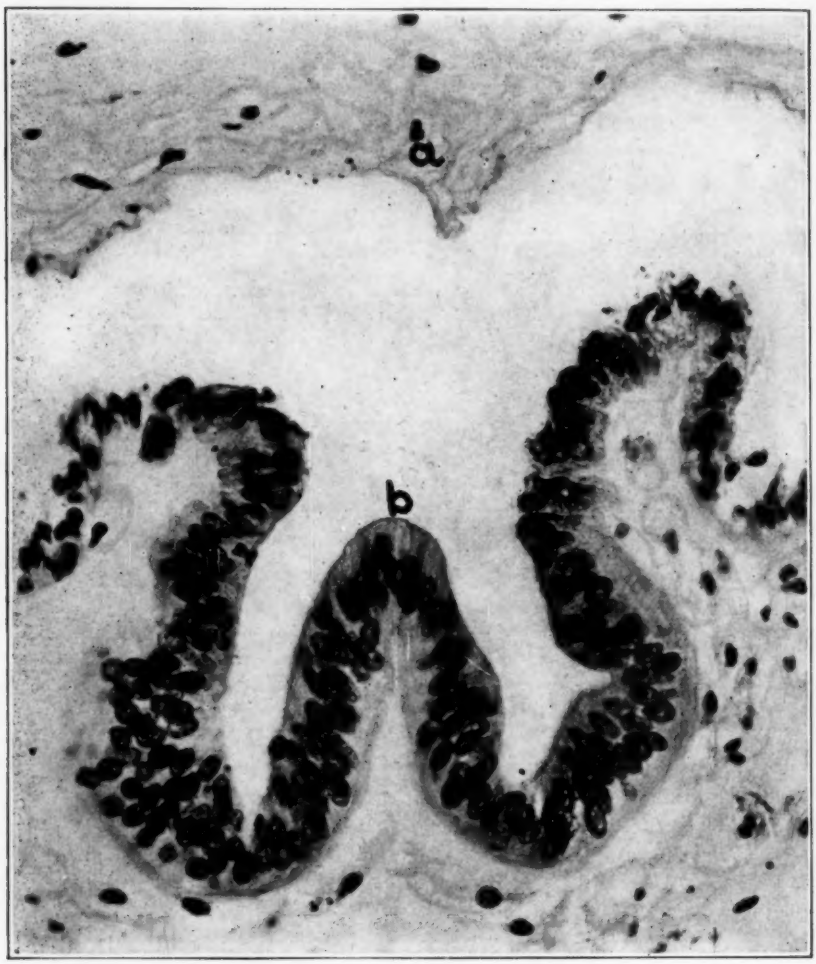



Fig. 5.—Microscopic section from *B* in figure 3, showing lens (*a*) and retinal epithelium near the ora serrata (*b*).

A report of a social worker in 1943 stated that the child had become obstinate and occasionally had attacks of a convulsive nature. He was placed in a state institution at the age of 4 years because his mother was unable to care for him adequately and because it was believed that his presence in the home would have a bad effect on the other child, who was normal. Report of an examination made in May 1945 follows:

"K. is a restless, overactive, mischievous boy. His head and face are asymmetric. The left nostril is absent; the right is apparently normal. The left eyebrow now extends along the left side of the nose. The left eye is absent and the orbit is covered with skin; there is a small sinus at the inner angle, through which lacrimation takes place. There is some loss of use of the right hand, which he holds in a

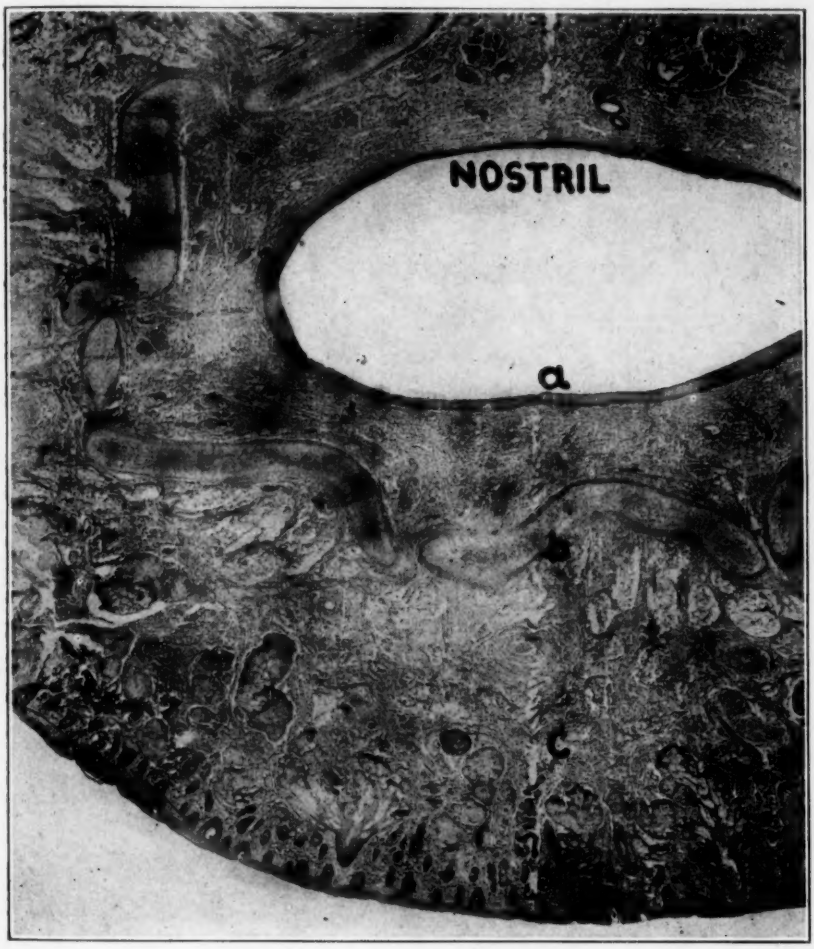



Fig. 6.—Proboscis. Microscopic section of the nostril, showing the lumen. Present are the mucosa (*a*), cartilage (*b*) and skin (*c*), which is normal.

flexed position. His gait is defective. Reflexes are exaggerated on the right side. He can understand simple verbal material and can say a few very simple words indistinctly. His reaction time is rapid. Memory is poor. His basal mental age is 12 months, and the upper limit, 3 years, with one test passed at this level. He failed in all four tests. His intelligence quotient, of 41 (Kuhlman), was determined on the basis of his actual age. He plays fairly well with the other boys in his ward.

There is still drainage from the left lacrimal duct. His behavior is improving, and he seems more amenable to direction than at the time of admission."

This case presents a combination of four anomalies: cyclopean eye; lateral proboscis; cleft palate, with normal half-face, and cleft lip. The

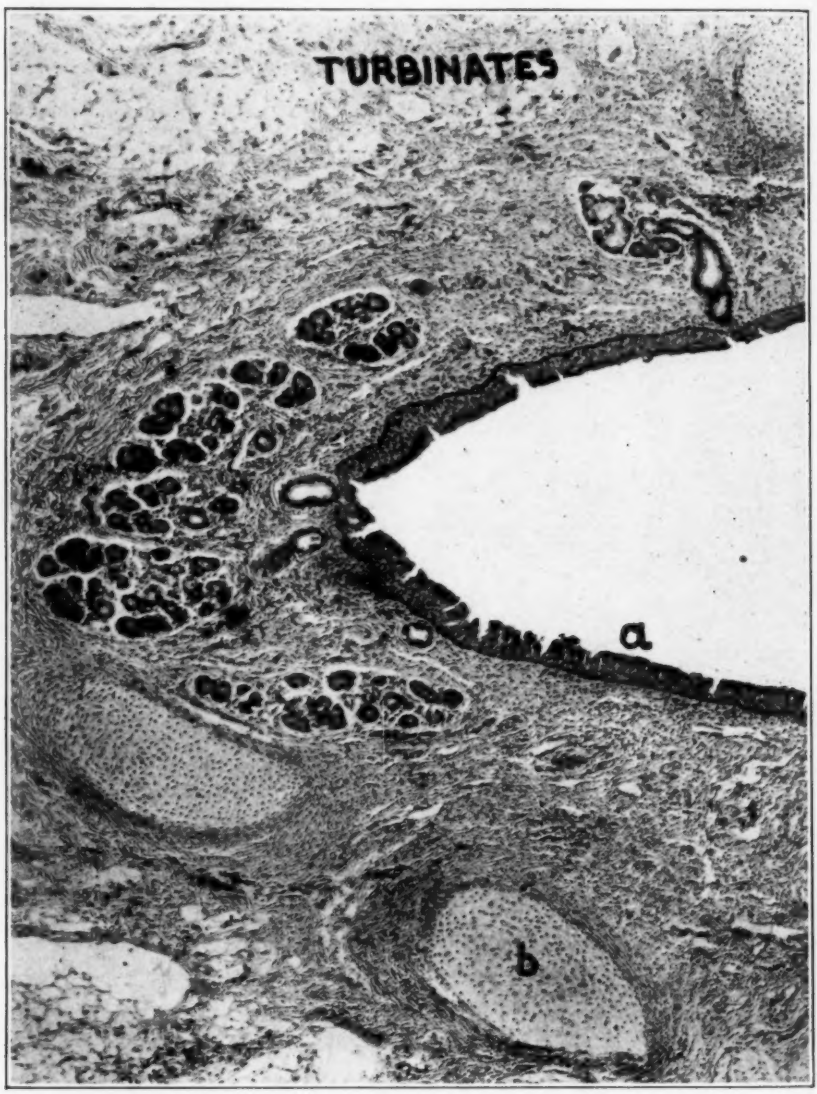



Fig. 7.—Proboscis. Microscopic section of the turbinate processes, showing the lumen. Present are mucosa (*a*), which is normal, and cartilage (*b*), of fetal type.

literature has several references to cases in which two of these anomalies have occurred together. The only previous case in which all four

were present is that reported by Rating,[13] which, however, differed from the present case in that there were two eyes in addition to the double cyclopean eye.

With few exceptions, malformations may be fitted into a graded series. In only 3 of the reported cases has the presence of three eyes or eye sockets been proved by dissections of the skull in a single person. As our case falls into this unique group, we shall review these cases individually.

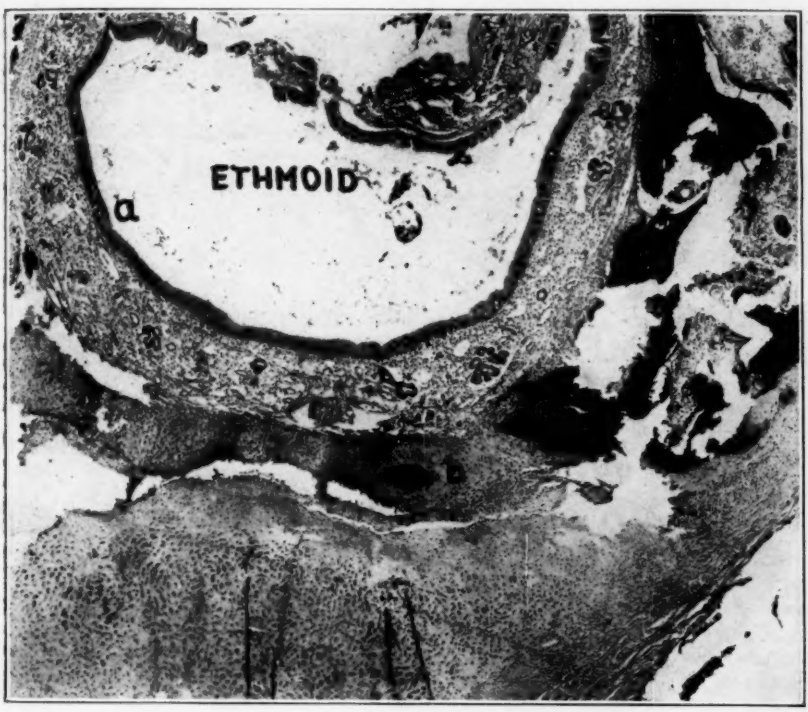



Fig. 8.—Proboscis. Microscopic section of the ethmoidal region, showing lumen. Present are mucosa (*a*) and cartilage with bone (*b*), which is normal.

1. Förster's[12] case (1861) was that of a girl aged 8 months. There were two eyes and a central, well formed, half-nose. Between the eyes there was a depression, beneath which was a cavity surrounded by eyelids with eyelashes and lined with conjunctiva, but there was no eye. The skull had a rudimentary central orbit and two extra frontal bones (fig. 9).

2. Rating's[13] case (1933) has no duplicate in the literature. The fetus had one right and one left eye and two noses. Under the extra nose at the right there was a cyclopean double eye. There were also

double cleft lip and cleft palate. There were three orbital cavities in the skull (fig. 9).

3. Bimar's [15] case (1888), an extraordinary one also, was that of a woman who lived to be 52. The depression in the skin above and between the two noses marked an orbital cavity between the two orbits containing the right and the left eye, but the third orbit contained no eye. This peasant woman led a normal life and was self supporting. The author suggested incomplete twinning as the causal factor (fig. 9).

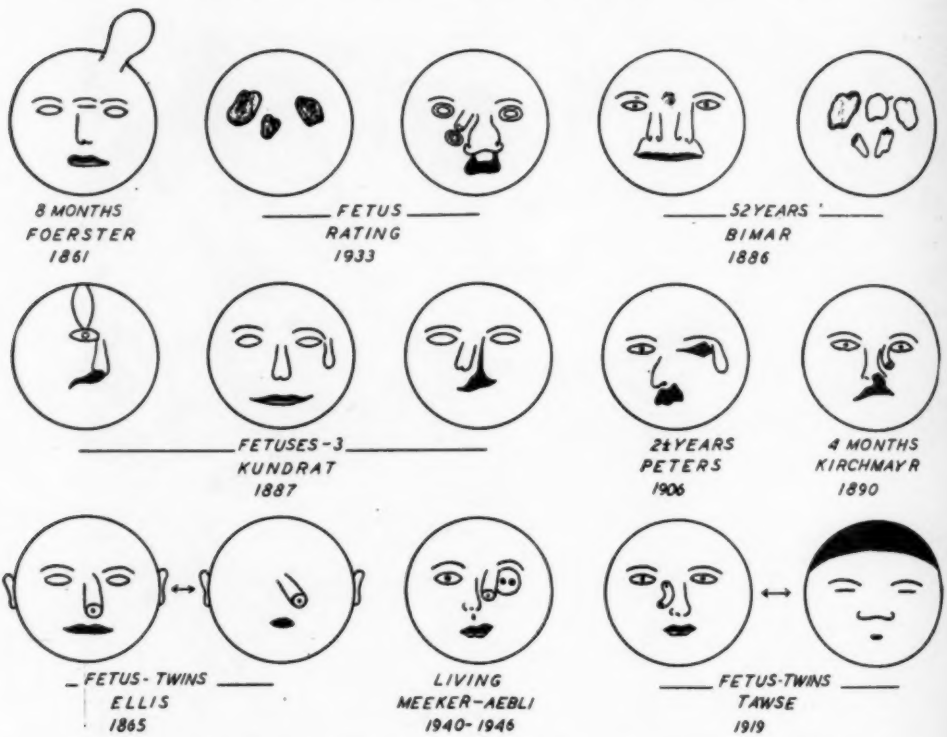



Fig. 9.—Chart illustrating the cases cited in the text to indicate the relationship of lateral proboscis, cyclopean eye, cleft palate and atypical monozygotic twinning. Isolated, rarer, cases of persons with three eyes or three eye "sockets" are also known.

4. Lehmann-Nitsche's [16] case (1901) was that of a youth aged 18 and was similar to Bimar's case. This youth had sufficient intelligence to earn his living as a farmer but was constantly in trouble with the police.

15. Bimar: Note sur un monstre pseudencéphalien, Gaz. hebd. d. sc. méd. de Montpelier **8**:349 and 385, 1886.

16. Lehmann-Nitsche, R.: Ein seltener Fall von angeborener medianer Spaltung der oberen Gesichtshälfte, Virchows Arch. f. path. Anat. **163**:126, 1901.

5. Kirchmayr's [17] case (1906), that of a girl 4 months old, showed the association of lateral proboscis and coloboma of the lids, cleft lip and cleft palate (fig. 9).

6. Selenkoff's [18] case, that of a man aged 54, is interpolated here to illustrate the lateral proboscis and the upper lid and eyebrow continuing along the nose, the latter coming under the heading of Gesell's atypical twinning processes. Our patient now shows the same growth of the eyebrow.

## COMMENT

Our case may be considered from the standpoint of the four associated malformations, namely, cyclopean eye, lateral proboscis, cleft palate and cleft lip.

Cyclopean eye, occurring in association with cleft palate, coloboma of the lids and in monozygotic twinning, and rarely with polydactyly, has been reported by Kundrat,[19] Rating [13] and van Duyse.[20] Arey,[21] Fuchs,[22] Duke-Elder,[23] Pires de Lima [24] and Gesell and Blake [25] were convinced that the cyclopean eye is an expression of monozygotic twinning.

Lateral proboscis in combination with cleft palate and coloboma of the ocular tunics and lids and in monozygotic twinning has been reported by Kundrat,[19] Peters,[26] Tendlau,[27] van Duyse [28] and Tawse.[29] Lateral proboscis and cleft palate, occurring singly or in combination, are accepted as hereditary (Arey [21] and Thoma [30]).

---

17. Kirchmayr, L.: Ein Beitrag zu den Gesichtsmissbildung, Deutsche Ztschr. f. Chir. **81**:71, 1906.

18. Selenkoff, A., cited by Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1921-1938, vol. 3, pt. 1, p. 56, fig. 52.

19. Kundrat: Ueber Nasen- und Gesichtsspalten, München. med. Wchnschr. **34**:90, 1887.

20. van Duyse: Pathogénie de la cyclopie, Arch. d'opht. **18**:481, 581 and 623, 1898.

21. Arey, L. B.: Developmental Anatomy, ed. 4, Philadelphia, W. B. Saunders Company, 1940.

22. Fuchs, E.: Text-Book of Ophthalmology, translated by A. Duane, ed. 7, Philadelphia, J. B. Lippincott Company, 1923.

23. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1244.

24. Pires de Lima, J. A.: Monstros ciclocefalianos, Folia anat. univ. conimb. (art. 14) **15**:1, 1940.

25. Gesell, A., and Blake, E. M.: Twinning and Ocular Pathology, with a Report of Bilateral Macular Coloboma in Monozygotic Twins, Arch. Ophth. **15**: 1050 (June) 1936.

26. Peters, A.: Ueber die bei Missbildungen des Gesichtes vorkommende Rüsselbildung, Ber. ü. d. Versamml. d. ophth. Gesellsch. **36**:163, 1911.

*(Footnotes continued on next page)*

Cleft palate has frequently occurred in conjunction with cyclopean eye and lateral proboscis, in identical twins (Kundrat,[19] Heinonen,[31] Tawse,[29] and Ellis [32] and with polydactyly (Birkenfeld [33]).

The hereditary factor is also important in cleft lip, for Schröder [34] found a hereditary factor in 42.7 per cent of cases, in 75 per cent of which it was recessive and in 25 per cent dominant. Additional evidence of hereditary influence was supplied by Klopstock,[35] van Duyse,[20] Schröder,[34] Haymann,[36] Thoma,[30] Saunders [37] and Rating,[13] who suggested that inheritance of cleft lip followed the mendelian law, and Redenz [14] expressed the same opinion about cyclopean eye and the central proboscis.

It is of particular interest that these anomalies are often associated with monozygotic twinning. The suggestion has been made that partial fusion of twins results in a person with duplication of features. A better explanation, however, is that there is incomplete separation of monozygotic twins, as suggested by Ellis [32] and Tawse [29] (fig. 9). This explanation does not weaken the theory of the influence of heredity but, rather, strengthens it, for monozygotic twinning is itself probably under hereditary influences (Newman,[38] Gesell and Blake,[25] Thoma [30]). Two remarkable examples of hereditary influence in twinning (Newman [38]) are afforded by the Picard and Rubin families, in which the parents on both sides were uniovular twins and uniovular twins were born into both families.

---

27. Tendlau, A.: Ein Fall von Proboszis lateralis, Arch. f. Ophth. **95**:135, 1918.

28. van Duyse, G. M.: Proboscide latérale et colobome oculaire atypique avec lenticome postérieur, Arch. d'opht. **36**:463 and 555, 1919.

29. Tawse, H. B.: Supernumerary Nostril and Cavity, Proc. Roy. Soc. Med. (Sect. Laryng.) **13**:28, 1919-1920.

30. Thoma, K. H.: Oral Pathology, St. Louis, C. V. Mosby Company, 1941.

31. Heinonen, O.: Ueber die Refraktion bei eineiigen Zwillingen, speziell in Hinsicht der asymmetrischen Fälle, Acta ophth. **2**:35, 1924.

32. Ellis, R.: On a Rare Form of Twin Monstrosity, Tr. Obst. Soc. London **7**:160, 1865.

33. Birkenfeld, W.: Ueber die Erblichkeit der Lippenspalte und Gaumenspalte, Arch. f. klin. Chir. **141**:729, 1926.

34. Schröder, C. H.: Untersuchungen über die Vererbung der Hasenscharte und Gaumenspalte mit besonderer Berücksichtigung des Erbgangs, Arch. f. klin. Chir. **182**:299, 1935.

35. Klopstock, A.: Familiäres Vorkommen von Cyklopie und Arrhinencephalie, Monatschr. f. Geburtsh. u. Gynäk. **56**:59, 1921.

36. Haymann, A. T.: Amniogene und erbliche Hasenscharten, Inaug. Dissert. (Leipzig), Berlin, L. Schumacher, 1903.

37. Saunders, J.: De erfelijkheid van hazelip en gespleten verhemelte, Tijdschr. v. tandheelk. **41**:439, 1934.

38. Newman, H. H.: Multiple Human Births, American Association for the Advancement of Science Series, New York, Doubleday, Doran & Company, Inc., 1940.

Consideration of the present case thus shows that in each of the four associated anomalies heredity is known to play an important role and that their association with atypical monozygotic twinning is more than an accidental occurrence.

On the basis of this discussion, the suggestion is made, therefore, that the anomalies in this case are the result of incomplete separation of monozygotic twins and that hereditary influences are important factors in their development.

SUMMARY

A case is reported in which cyclopean eye, lateral proboscis, cleft palate and cleft lip are associated. There is no case in the available literature in which these anomalies have been associated in the manner described, and ours is the only case of cyclopean eye in which the child has lived to the age of 5½ years.

Comparison of this case with the cases previously reported strongly suggests that the defects are the result of incomplete separation of monozygotic twins. Hereditary influences are of importance not only in the occurrence of the individual anomalies but in the formation of the twins on which their development depends.

30 East Fortieth Street.

# SPECIFIC TREATMENT OF OCULAR BURNS DUE TO LEWISITE ($\beta$-CHLOROVINYLDICHLOROARSINE)

IRVING H. LEOPOLD, M.D.
AND
FRANCIS HEED ADLER, M.D.
PHILADELPHIA

RECENTLY Peters,[1] in England, and Waters and Stock,[2] in the United States, have presented information concerning an effective antiarsenical agent, BAL (2, 3-dimercaptopropanol), which was discovered and developed during the war years. It has been shown not only to be an effective therapeutic agent against arsenical war agents but also to be of value in the treatment of the various types of arsenical poisonings encountered in civilian practice.

It is the purpose of this review to give a brief summary of the development of BAL for ocular therapeutic use.

## PHYSICAL AND CHEMICAL PROPERTIES

Among the early forms of BAL tested for therapeutic effect in the eye in this country were NDR 133-J, NDR 133-N, NDR 133-Q-Z, NDR 133-5, NDR 133-11 and NDR 133-12.[3] These were all 2, 3-dimercaptopropanol of varying degrees of purity and prepared by different modifications in the chemical process. Composites of later preparations of BAL were NDR 133-26 and NDR 133-27, and one composite lot, NDR 133-28, is now known as American Reference Standard (ARS) BAL. This compound must meet definite physical and chemical requirements,[4] with respect to such factors as $p_H$, color, refractive index, bromine content, thiosulfur content and heat stability. In addition, its toxicity must not exceed a certain minimum, and it must possess a standard therapeutic efficiency.[4]

---

From the Department of Ophthalmology of the Hospital of the University of Pennsylvania.

The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania.

1. Peters, R. A.; Stocken, L. A., and Thompson, R. H. S.: Nature, London **156**:616 (Nov. 24) 1945.

2. Waters, L. L., and Stock, C.: Science **102**:601 (Dec. 14) 1945.

3. N D R stands for National Defense Research Committee.

4. Calvery, H. O.; Braun, H. A.; Draize, J. H.; Woodward, G.; Vos, B.; Fassett, D.; Fitz Hugh, O., and Whiteman, G.: Personal communication to the authors, April 1943.

American Reference Standard BAL is a clear, colorless fluid with a pungent and disagreeable odor. It is soluble in vegetable oils, alcohols and water up to 7 per cent and is freely soluble in various organic solvents. The most used solvents for ocular use have been ethylene and propylene glycol, ethyl phthalate, water and "cellosolve" (ethylene glycol monoethyl ether).

BAL is readily oxidized. It is oxidized more rapidly in water than in ethylene glycol and more rapidly in dilute than in concentrated solution.[5] It is readily oxidized by minute quantities of iron or copper.[6]

The American Reference Standard BAL produces a clear 5 per cent aqueous solution.[7] However, the aqueous solution of ARS BAL, like others, shows cloudiness and even droplet separation on standing; these droplets are probably polymers of BAL.[8]

### TOLERANCE OF EYES TO BAL

All the forms of BAL listed in the preceding section have been tested for ocular tolerance in rabbits.[9] The later preparations of BAL have also been tested in monkeys [9b] (September communication) and in human subjects.[10] Concentrations as low as 5 per cent will produce conjunctival injection, blepharospasm and lacrimation. The symptoms may be severe enough to render a man a casualty for as long as fifteen minutes, although the severest blepharospasm usually lasts only two to five minutes.[11] A few drops of 5 per cent aqueous solution of BAL or 0.1 cc. of an ointment containing BAL in 5 per cent concentration may cause a conjunctival injection lasting an hour. Visual function probably will not be greatly influenced longer than fifteen minutes after application. By increasing the concentration from 5 to 10 per cent, one increases the amount and degree of conjunctival irritation but fails to produce any permanent corneal damage in rabbit eyes.[9]

Concentration of BAL above 20 per cent may produce irreparable corneal damage; the eyes may eventually heal but with scar formation. If concentrations higher than 25 to 30 per cent are used, many of the eyes will fail to heal sufficiently to leave function.

---

5. Adler, F. H.; Leopold, I. H.; Steele, W. H., and Crandall, A. S.: Personal communication to the authors, January 1943.

6. Barron, G.: Personal communication to the authors, June 1943.

7. (*a*) Adler, F. H.; Leopold, I. H., and Steele, W. H.: Personal communication to the authors, June 1942. (*b*) Calvery and others.[4]

8. Brubaker, M. M.: Personal communication to the authors, August 1942.

9. (*a*) Adler, F. H.; Leopold, I. H., and Crandall, A. S.: Personal communication to the authors, April and July 1942. (*b*) Hughes, W.: Personal communication to the authors, June and September 1942. (*c*) Calvery and others.[4]

10. Adler, F. H.; Leopold, I. H.; Steele, W. H., and Crandall, A. S.: Personal communication to the authors, December 1942. Hughes.[9b]

11. (*a*) Barr, J., and Sulzberger, M.: Personal communication to the authors, July 1943. (*b*) Lazier, W. A., and Salzberg, P. L.: Personal communication to the authors, July 1943.

These results are the same regardless of whether the material is administered in the form of drops or as an irrigant, when a total of 2 cc. is used.[12] Continuous use of any BAL was found to be harmful to both the normal eye and to an eye burned with lewisite (β-chlorovinyldichloroarsine). If BAL, for example, is used twice daily for several days on lewisite-burned eyes, the eyes will remain inflamed until the BAL therapy is stopped and will then clear in twenty-four to thirty-six hours.[9a] It has been reported that the reactions produced by concentrations of BAL over 5 per cent in eyes previously exposed to lewisite are severer than those produced by BAL on the normal cornea and that this indicates that lewisite lowers the tolerance of the cornea for BAL. This action is probably not specific, since to an eye inflamed by any irritant other than lewisite BAL is more irritating than, to a normal eye.

### SENSITIVITY OF OCULAR TISSUES TO BAL

Attempts to induce hypersensitivity to BAL in eyes of rabbits by repeated applications have failed in normal eyes, as well as in eyes previously exposed to lewisite and treated with BAL.[13] This does not necessarily mean that human eyes may not become sensitive, for rabbits are notoriously poor animals on which to perform experiments on acquired sensitivity. Sulzberger has demonstrated a type of hypersensitivity of human skin to BAL.[11a]

### THERAPEUTIC EFFECTIVENESS OF BAL

After the fundamental investigations of Stocken and Thompson[14] that led to the use of BAL for lesions of the skin produced by lewisite, Mann and her associates[15] were the first to evaluate BAL as a therapeutic agent for ocular lesions. In view of the excellent results on ocular injuries due to lewisite obtained by many British workers, BAL was tried in the United States.[9a] Work done with previously recommended therapeutic agents for lesions due to lewisite, such as hydrogen peroxide and potassium permanganate, conclusively proved the superiority of BAL.[16] After the efficacy of this compound had been demonstrated, the following points had to be considered:

12. Adler, F. H.; Leopold, I. H.; Steele, W. H., and Crandall, A. S.: Personal communication to the authors, February 1943.

13. Adler, F. H.; Leopold, I. H.; Steele, W. H., and Crandall, A. S.: Personal communication to the authors, November 1942.

14. Stocken, L. A., and Thompson, R. H. S.: Personal communication to the authors, 1941 and 1942.

15. (*a*) Mann, I., and Pirie, A.: Personal communication to the authors, 1941 and 1942. (*b*) Clarke, A. J.: Personal communication to the authors, 1941 and 1942. (*c*) Robson, J. M., and Scott, G. I.: Personal communication to the authors, 1941 and 1942.

16. Mann, I., and Pirie, A.: Personal communication to the authors, 1941 and 1942. Adler, F. H.; Leopold, I. H., and Crandall, A. S.: Personal communication to the authors, April and May 1942.

*Time of Initial Application.*—BAL was found to give excellent results when used within five minutes after contamination of the eyes with lewisite.[17] The majority of eyes treated within five minutes can be expected to show at the most only slight residual corneal damage after doses of lewisite which uniformly cause perforation in eleven days. The residual damage is usually a nebula or the macular type of small scar. The longer the interval before BAL is applied to the lewisite-burned eye, the less its effectiveness. Although the effectiveness of BAL decreases rapidly after ten to twelve minutes,[18] there is still some effect after thirty minutes.[19] Occasionally eyes will be benefited as late as forty-five minutes after contamination,[9a] but use of BAL one hour after contamination has no beneficial effect in experiments with the doses previously described.

*Repetition of Application.*—There is evidence that better therapeutic results will be obtained by applying the drug once after the initial application. This is of particular value in cases in which, for any reason, the casualty has not placed enough BAL in his eye on the first application.[20]

*Vehicles for BAL.*—Solvents Considered: All the early work with BAL was done with the drug in liquid vehicles. BAL was used in thiodiglycol (2,2'-dihydroxyethyl sulfide) by Mann and other workers.[15a] Glycol was used both by American [21] and by British workers.[15a] Hughes[9b] tested propylene glycol and glyceryl triacetate. Calvery and others [4] tried dimethyl phthalate and diethyl phthalate. Water has also been shown to be a suitable vehicle.[22]

Influence of Solvent on Therapeutic Results: It was shown that water as a solvent gave the best therapeutic results,[4] but such aqueous solutions are not stable.[5] Calvery and associates [4] demonstrated that solutions in ethylene glycol were slightly more effective therapeutically than solutions in propylene glycol, both of which were more stable than aqueous solutions.

*Toxicity of Solvent.*—Water is readily tolerated by the rabbit's cornea,[23] while ethylene glycol is less irritating than propylene glycol. The phthalates are somewhat less toxic than ethylene glycol.[4] However, none of these solvents produces irreparable damage.

---

17. Calvery and others.[4] Footnote 9 *a* and *b*. Mann and Pirie.[15a]

18. Calvery and others.[4] Hughes.[9b] Mann and Pirie.[15a]

19. Footnote 9 *a* and *b*. Mann and Pirie.[15a]

20. Adler, F. H.; Leopold, I. H.; Steele, W. H., and Crandall, A. S.: Personal communication to the authors.

21. (*a*) Calvery, H. O.; Braun, H. A.; Vos and Fassett: Personal communication to the authors, July 1943. (*b*) Calvery and others.[4] (*c*) Adler and others.[9a]

22. Calvery and others.[4] Adler and others.[9a]

23. Adler, Leopold, Steele and Crandall.[20] Adler, Leopold and Crandall.[9a]

*Penetrating Ability of BAL in Solvents.*—With a basic bismuth dithiosalicylate ("thiol") titration method, the penetration of BAL in various solvents into the aqueous was determined.[5] It was found that BAL penetrates most rapidly in water. BAL in ethylene glycol and "cellosolve" does not reach the aqueous so quickly, although all solvents of 5 per cent concentration give adequate therapeutic aqueous levels within the first five minutes. This greater penetration of BAL in water may account for the better therapeutic results reported.[5] These studies indicate that BAL penetrates rapidly enough to combat lewisite.

*Stability of BAL in Solvents.*—The foregoing data on solvents lead to the conclusion that water is the best solvent. However, iodine titration studies [5] have shown that BAL loses sulfhydryl groups in water much more rapidly than in ethylene glycol and that this deterioration takes place in dilute solutions more rapidly than in concentrated solutions.[5] Investigators [24] were unable to demonstrate any significant loss of therapeutic efficiency of a 5 per cent solution of BAL in ethylene glycol standing at room temperature for six to eight weeks. Calvery and associates[21a] also tested solutions of BAL in ethylene glycol at temperatures from freezing to 50 C. and after bubbling oxygen through the solutions; they concluded that solutions of BAL in ethylene glycol will retain their full therapeutic efficiency for considerable periods under the temperatures and exposures to air likely to be encountered in practice.

Various attempts to add preservatives to solutions of BAL in ethylene glycol have shown that these substances do not reduce its therapeutic efficiency.[4] The agents used were thiamine hydrochloride, 0.028 per cent, and ascorbic acid, 0.028 per cent, in a 5 per cent solution of BAL in ethylene glycol. Since solutions with a $p_H$ below 6 are more stable than those with a $p_H$ above 6, boric acid was used in the same preparations. Although resultant products are slightly more stable, there is probably no real necessity for their employment. No therapeutic difference could be demonstrated by using BAL solutions at $p_H$ 3, 4, 5, 6.8, 7.8 and 8. The $p_H$ of American Reference Standard BAL is 5.8, which therefore does not require alteration for effectiveness or stability.[21a]

*Ointment Bases.*—BAL has been found to be therapeutically effective in many ointment bases after the initial observation on its action in the Friedenwald-Fuqua formula.[25] Petrolatum,[26] K-Y lubricating jelly N.N.R., "aquaphor" (an oxycholesterol-petrolatum ointment base) and

24. Adler, F. H.; Leopold, I. H.; Steele, W. H., and Crandall, A. S.: Personal communication to the authors, October 1942. Calvery and others.[21a]

25. Hughes.[9b] Friedenwald-Fuqua ointment consists of benzyl benzoate, 5 per cent; peanut oil, 37 per cent; wool fat, 8 per cent; cetyl alcohol, 10 per cent; glyceryl monostearate, 10 per cent; white petrolatum U. S. P. 25 per cent.

26. Friedenwald, J., and Hughes, W.: Personal communication to the authors, February 1942. Stocken and Thompson.[14]

vanisol ointment [27] are other bases that have been used. However, the earlier work with ointments found them to be not quite so effective as liquid preparations.[28] Efforts were made to find an ointment which would stand wide changes in temperature, exposure, and so forth,[11] and at the same time give minimum therapeutic performance and meet standard biologic requirements. Many ointments were tried,[11] and after numerous tests the following ointments were chosen as satisfactory:

| | Percentage |
|---|---|
| **1. United States Navy (no. 13)** | |
| Peanut oil | 36.95 |
| Wool fat U. S. P. | 8.0 |
| Cetyl alcohol | 10.0 |
| Glyceryl monostearate | 10.0 |
| White petrolatum, soft, U. S. P. | 25.0 |
| Benzyl benzoate | 5.0 |
| Mixed tocopherols | 0.05 |
| Medicament | 5.0 |
| **2. United States Army (no. 14)** | |
| Boric acid | 1.898 |
| "Carbowax 4000"* | 7.592 |
| "Carbowax 1500"* | 47.45 |
| Ethylene glycol | 37.96 |
| Isoascorbic acid | 0.05 |
| Thiamine hydrochloride | 0.05 |
| Medicament | 5.00 |
| **3. British (D 20)** | |
| Diethyl phthalate | 10.0 |
| Wool fat U. S. P. | 80.0 |
| BAL | 10.0 |

* "Carbowax" compounds are polyethylene glycols of high molecular weight.

McLean and Cuthbert [11] showed that these ointments are as effective therapeutically as liquid preparations in equal concentrations, but Calvery, cited by others,[11a] still found the standard solution to be slightly superior to the ointments. These investigators demonstrated the low ocular irritancy of these ointments in animals and in human subjects, cited by Lazier and Sulzberger.[11b] It has been shown also that BAL in ointment may be applied with good therapeutic results in experimental animals [29] by rubbing it on the lids, making certain that some gets between them. Because of the oxidation of BAL in the presence of iron or copper, ointment must be stored in lead tubes or in glass.

### CONCENTRATION

BAL has been shown to be effective against ocular lesions due to lewisite at 20 per cent,[30] 10 per cent,[17] 5 per cent,[9a,b] and 3 per cent.[31] Three per cent and 5 per cent solutions of BAL give just as effective a therapeutic response as a 10 per cent solution.[31] These results indicate

27. Adler and others.[10] Vanisol consists of sodium stearate, 20 per cent; cetyl alcohol, 5 per cent; glyceryl monostearate, 8 per cent; and water, 67 per cent.

28. Calvery and others.[21a] Adler and others.[10]

29. Adler and others.[10] Mann and Pirie.[15a]

30. Adler and others.[9a] Mann and Pirie.[15a]

31. Calvery and others.[4] Hughes.[9b]

that the excess of BAL over that needed for neutralization in the 5 per cent solution has no demonstrable therapeutic value, but when solutions of this strength are prepared the excess does allow for deterioration and is of value from this standpoint. No significant therapeutic difference could be demonstrated between instillation of 2 to 4 drops of 5 per cent solution of BAL in ethylene glycol and irrigation with 1 cc. of the solution.[8a] It is recognized by all workers in this field that 2 drops of a 3 or 5 per cent solution furnishes a large excess of BAL over that required to react with the lewisite likely to be present in the eye.

### MODE OF APPLICATION

There are thus two forms, liquid and ointment, in which BAL can be successfully applied to the eye of the experimental animal. It remained to show which was the more practical for use in the field under actual battle conditions. Would it be easier for the soldier under conditions of battle to use an ointment in his eyes or a liquid? A series of tests was undertaken at the Edgewood Arsenal,[32] using volunteers and putting into their eyes a tear gas of sufficient concentration to cause lacrimation and blepharospasm. After exposure to the tear gas, each subject was given either a tube of ointment or a container with liquid and instructed to place the contents into his eye. A solution of tetracaine hydrochloride was incorporated in both the liquid and the ointment, together with a solution of homatropine. The time was taken when the subject first gained relief from pain. Pupillary diameters were measured at intervals as a further check on the rapidity of action. It was found that it was far easier for the men to get the ointment into their eyes. In some cases a few drops of the solution was spilled out on the cheeks or on the ground and were lost, whereas with the ointment, if there was difficulty in getting it into the eye, the portion remaining on the lids would eventually be rubbed in. Another advantage of the ointment is that the subject could get the ointment into his eye even when lying face down. Even if the ointment tube was dropped, it could be recovered from the ground.

### INFLUENCE OF ANESTHETICS

Repeated use of 1 per cent tetracaine hydrochloride four times daily has no deleterious effect on the course of ocular lesions due to lewisite treated with BAL.[8a]

### INFLUENCE OF BAL ON OCULAR LESIONS DUE TO WAR GASES OTHER THAN LEWISITE

BAL ointment has a specific effect not only on ocular lesions due to lewisite but also on those due to methyldichloroarsine,[33] ethyldichloro-

32. Friedenwald, J.; Woods, A., and Adler, F. H.: Personal communication to the authors, April 1943.

33. Mann, I.: Personal communication, 1942.

arsine [33] and phenyldichloroarsine,[34] and it has slight beneficial effect on lesions due to mustard gas (diethyl sulfide) when used immediately after contamination of the eyes. The BAL ointment has been shown to have a beneficial effect on ocular lesions due to mixtures of lewisite and mustard gas,[35] both liquid and vapor, lewisite and various nitrogen mustards (general formula β-chloroethylamine) in liquid form [36] and liquid phenyldichloroarsine and mustard gas.[37] Irrigations have been shown to enhance the efficacy of BAL ointment against mixtures of mustard gas and lewisite when used a minute or two after applying BAL ointment.[38]

### DERIVATIVES OF BAL

Attempts have been made to find a compound less toxic locally to ocular structures and more therapeutically effective than BAL for ocular lesions due to lewisite. Many compounds have been tested [39] on the eye. None of these compounds has been significantly more effective. However, several have been found just as good. Examples of these are:

NDR 230.....2,3-dimercaptopropyl acetate
NDR 287.....S-(diethanolaminomethyl) ether of 1,2-dimercaptopropanol
NDR 288.....2-mercapto-3-(methyl glucamino methylmercapto)-propanol
NDR 298.....2,3-dimercaptopropyl ethyl ether
NDR 607.....2,3-dimercaptopropyl propionate
NDR 608.....2,3-dimercaptopropyl butyrate
KD 8..... 2-mercapto-3-(methylcarboxymethyl aminomethylmercapto)-propanol

There does seem to be no reason at present for adopting any of these derivatives for ocular use in preference to ARS BAL.

---

34. Davson, H., and Dunphy, E. B.: Personal communication to the authors, 1944. Sholz, R.: Personal communication to the authors, February 1944. Adler and associates.[7a]

35. (*a*) Mann, I., and Pirie, A.: Personal communication to the authors, March 1942. (*b*) McNamara, B. P.; Harrison, A. E., and Guberman, E. A.: Personal communication to the authors, July 1943. (*c*) Dunphy, E. B., and Uhde, G. I.: Personal communication to the authors, January 1944. (*d*) Cuthbert, M.: Personal communication to the authors, March 1944. (*e*) Calvery, H. O.; Braun, H. A., and others: Personal communication to the authors, August 1943. (*f*) Adler and associates.[7a]

36. Adler, F. H.; Leopold, I. H.; LaMotte, W. O., Jr., and Steele, W. H.: Personal communication to the authors, November 1943.

37. Laughlin, R. C.: Personal communication to the authors, December 1943.

38. Adler, F. H.; Leopold, I. H., and LaMotte, W. O., Jr.: Personal communication to the authors, February 1944.

39. Adler, F. H.; Leopold, I. H.; Steele, W. H., and Crandall, A. S.: Personal communication to the authors, July 1943. Zingero, F. F.; McNamara, B. P., and Harrison, A. E.: Personal communication to the authors, 1943. Calvery and others.[21a]

# USE OF PRESERVED CARTILAGE IN PLASTIC SURGERY OF THE EYE

SIDNEY A. FOX, M.D.
NEW YORK

THE USE of preserved cartilage in plastic surgery is not new. As Peer [1] pointed out, this procedure was reported on more than fifty years ago but it gradually fell into disuse. Recently it has been revived, and several surgeons have reported excellent results with isografts of preserved cartilage. Thus, Brown [2] has used cartilage preserved in alcohol since 1928, with satisfaction in most cases. Peer [3] has used the same material to repair depressions in the brow, orbital socket, skull and nose. Pierce and O'Connor [4] employed cartilage preserved in solution of merthiolate in 182 cases, with excellent results. O'Connor [5] reported 375 cases in which "pickled" cartilage was used and expressed enthusiasm for its use.

The advantages of using isografts of preserved cartilage instead of autografts of fresh cartilage are manifold and have been well covered in the literature previously cited. They may be enumerated as follows:

1. The material is easily obtained in any desired quantity, since autopsy material is always available. Furthermore, under proper conditions it may be kept for use as long as two years.

2. The danger associated with obtaining autografts is obviated. Granted that the obtaining of rib cartilage is neither particularly dangerous nor technically difficult, it is nevertheless, a procedure to which some patients understandably object. I have found this to be especially true of war casualties, many of whom have sustained multiple wounds and who object to further extensive operations which might be avoided.

---

1. Peer, L. A.: The Fate of Living and Dead Cartilage Transplanted in Humans, Surg., Gynec. & Obst. **68**:603-610, 1939.

2. Brown, J. B., cited by Peer, L. A.: Cartilage Transplanted Beneath the Skin of the Chest in Man, Arch. Otolaryng. **27**:42-58 (Jan.) 1938.

3. Peer, L. A.: Buried Grafts Used to Repair Depressions in the Brow, Eye Socket, Skull and Nose, J. M. Soc. New Jersey **35**:601-605, 1938.

4. Pierce, G. W., and O'Connor, G. B.: Reconstruction Surgery of the Nose, Ann. Otol., Rhin. & Laryng. **47**:437-452, 1938.

5. O'Connor, G. B.: Merthiolate: A Tissue Preservative and Antiseptic, Am. J. Surg. **45**:563-565, 1939.

3. The period of hospitalization and discomfort is shortened.

4. Isografts of cartilage show less tendency than autografts to bend or curve; they heal with firmer union with the surrounding tissues and resist infection better.[4]

Preservation of the material is simple and is based on the method first suggested by Pierce and O'Connor [4]: When obtained at autopsy, the cartilage is cleaned of all attached tissue, including the perichondrium. It is then placed in a solution composed of 2 parts of aqueous solution of merthiolate 1:1,000 and 2 parts of isotonic solution of sodium chloride for forty-eight hours. It is then transferred to a similar fresh solution daily for three days, being cultured before each transferral and cleaned of all adherent strands of perichondrium which might have been overlooked originally. These strands have a tendency to separate after the cartilage has soaked for several days. Rarely do cultures show any growth after the first forty-eight hours. After three successive sterile cultures, the material is stored permanently at ice box temperature in a solution of 1 part of aqueous solution merthiolate 1:1,000 and 3 parts of isotonic solution of sodium chloride. Two successive daily sterile cultures are obtained before the graft is used. I have seen the material stored for several months and have found it excellent for use. O'Connor [5] has used material stored as long as two years.

Preserved cartilage is about as easy to work with as fresh cartilage. It has a tendency to become brittle when exposed to the air too long and should therefore be moistened with saline solution from time to time at the operating table. Otherwise it is as firm and elastic as fresh cartilage and is excellent for grafting purposes. I have used it in 17 cases with what I consider good results. In 4 of these cases preserved cartilage was used as a substitute for the tarsal plate in reconstruction and repair of the lid. In 4 cases it was used to repair the bony contours around the orbit after fracture and deformity. In 5 cases it was used to raise the orbital contents after fracture of the orbital floor. Finally, it was used in 4 cases to fill in abnormal cavities in the empty socket caused by fracture.

For the sake of brevity, only that part of the repair which concerns the use of this material is described in the following case reports.

## REPORT OF CASES

*Repair of the Lids.*—Preserved cartilage was used in 4 cases of repair of the lid to replace lost tarsal cartilage.

CASE 1.—The patient had an anophthalmic left socket, fracture of the lateral wall of the orbit and loss of the outer halves of the lids and of the external canthus. Prior to admission he had had eight plastic procedures for repair of

the lids and socket. Figure 1 *A* shows partial repair of the left upper lid with a brow pedicle flap and partial repair of the lower lid with a forehead pedicle flap. This was his status on admission. The problem was to reconstruct the lids and the outer canthus. Figure 1 *B* shows the steps of the reconstruction, all done at one time. The remnants of the outer halves of the upper and lower lids of the left eye were split into two layers (fig. 1 *B*, *1*, solid line), and the conjunctiva was mobilized. The edges of the intact medial halves of the lids were freshened and united by a surgical tarsorrhaphy. The previously rotated, hair-bearing brow pedicle was raised and mobilized (fig. 1 *B*, 2). This pedicle was a bonanza, which is not often encountered in plastic surgery. The mobilized conjunctivas of the outer halves of the lids were united by a running 0000 plain surgical gut suture. A plate of preserved cartilage, measuring 15 by 12 by 1 mm., was sewed into position between the two lids to replace the lost tarsus (fig. 1 *B*, *2*, black rectangle). A sliding flap for reconstruction of the lower lid was then raised from the skin of the cheek and pulled up to complete the repair of the lower lid (fig. 1 *B*, *3*). The rectangle with the diagonal lines merely indicates the position of the cartilage plate between the skin and the conjunctiva

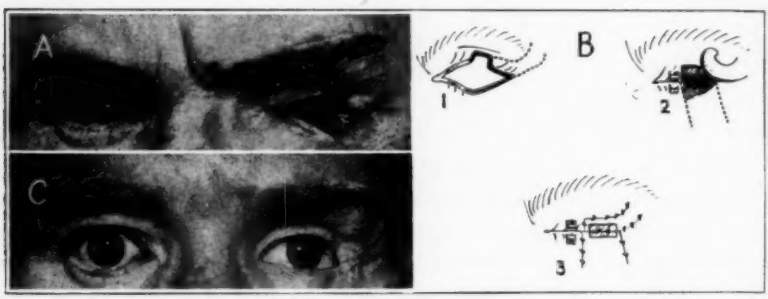



Fig. 1 (case 1).—*A*, appearance of the patient on admission. *B*, steps in the repair: *(1)* Outer halves of the lids are split, and the conjunctiva is mobilized. The margins of the inner halves of the lids have been freshened. *(2)* The inner halves of the lids are sutured together. The conjunctivas of the outer halves are united, and preserved cartilage graft is sewed in position (indicated by the black rectangle). Skin pedicles for reconstruction of the lids are raised. *(3)* Appearance on completion of operation, with skin pedicles sutured over the graft (indicated by the rectangle). *C*, result before revision of scars.

and does not show the exact size of the graft. Figure 1 *C* shows the result four weeks after removal of the tarsorrhaphy sutures and before revision of the scars.

Case 2.—On admission, the patient had an anophthalmic right socket with loss of the inner half of the right lower lid, as well as symblepharon (fig. 2 *A*). The first step in the repair was the fashioning of a small plate of preserved cartilage, measuring 12 by 5 by 1 mm. An incision was then made in the conjunctiva of the lower lid (fig. 2 *B*, *1*, vertical solid line) and the conjunctiva undermined nasally. The cartilage plate was then slipped into position, as shown. Two weeks later the conjunctival remnants of the medial portion of the lower fornix with its now adherent cartilage plate was dissected up. The medial half of the right upper lid was split into two layers just far enough to give two edges and was denuded of epithelium. The edges of the outer halves

of the lids were also denuded of epithelium and united by a tarsorrhaphy. The conjunctivas of the medial halves were united by a running suture of 000000 black silk, and a sliding flap of skin from the cheek was outlined and pulled up to complete the reconstruction of the skin of the lid (fig. 2 *B*, *2*). The skin flap was sutured to the skin-muscle layer of the medial half of the upper lid by a running suture of 0000 black silk (fig. 2 *C*). Six weeks later grafting of lashes from the opposite brow was done. The lids were separated six weeks

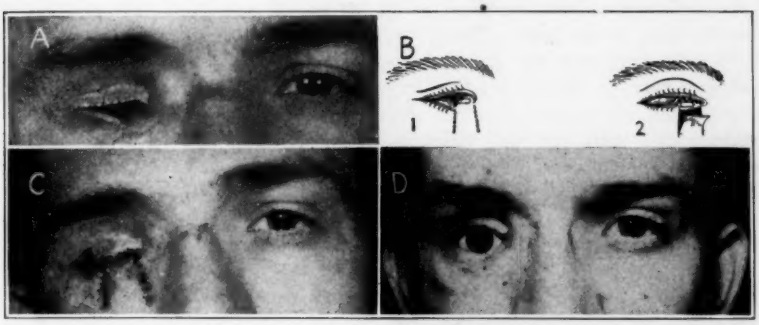



Fig. 2 (case 2).—*A*, appearance of the patient on admission. *B*, method of repair: *(1)* planting of preserved cartilage graft under the conjunctiva (broken rectangle); *(2)* reconstruction of the inner half of the lower lid (see text). *C*, appearance on the sixth day, before removal of the skin sutures. The tarsorrhaphy sutures were removed on the twelfth day. *D*, result. The lashes are beginning to grow.

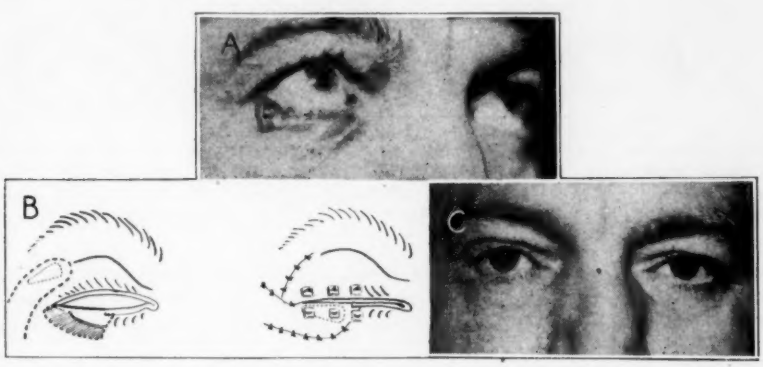



Fig. 3 (case 3).—*A*, tumor of the right lower lid. *B*, method of repair. (Left) Raising of delayed pedicle flap from the upper lid and planting of preserved cartilage graft. Excision of the full thickness lid with the tumor mass was done two weeks later. (Right) Appearance of lids on completion of repair. *C*, result nine days after separation of the lids.

later. The socket was shallow and had to be deepened by an additional mucous membrane graft, but the lid was adequate cosmetically and functionally (fig. 2 *D*).

CASE 3.—The patient gave a history of a growth on the right lower lid for twenty(?) years. There had been an appreciable increase in the size of this

growth during the last two years (fig. 3 *A*). As preliminary to the repair a pedicle flap was raised from the skin of the right upper lid, and a plate of preserved cartilage measuring 14 by 5 by 1 mm. was fashioned and slipped under the skin pedicle before it was sutured back into place (fig. 3 *B, 1*).

Fourteen days later the outer portion of the right lower lid was completely resected. The excised fragment of full thickness lid measured 16 by 15 mm. at its widest point. The edge of the remaining conjunctiva in the outer half of the lower fornix was undermined and mobilized. The edge of the outer half of the right upper lid was denuded of epithelium and split into two layers in order to give two edges. These were not mobilized. The conjunctiva from the lower fornix and the tarsoconjunctiva of the upper lid were united by a running suture of 000000 black silk. The pedicle flap previously fashioned in the upper lid was raised, together with its adherent cartilage plate. The under surface of the cartilage was found to be well vascularized. This pedicle was then swung down into the skin dehiscence of the lower lid and sutured into

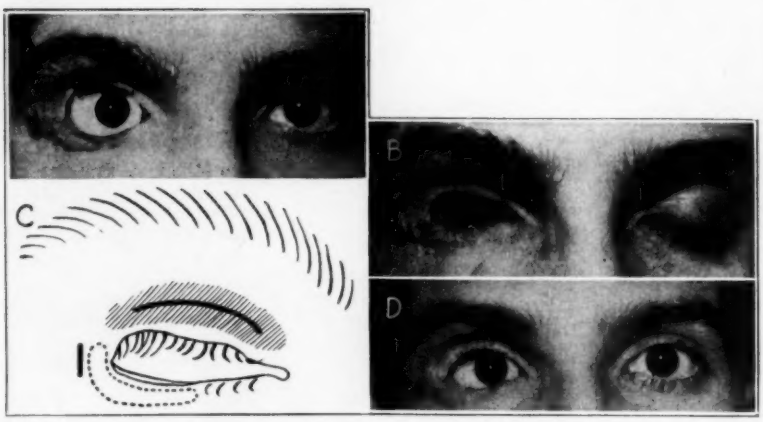



Fig. 4 (case 4).—*A*, lagophthalmos of the upper and lower lids of the right eye. *B*, same without prosthesis and with the eyes closed. *C*, position of cartilage plate grafted under the skin of the lower lid (dotted area). The solid vertical line shows position of the incision. D, appearance six weeks later.

position. Three mattress sutures of black silk tied over pegs furnished additional support to the lower lid and graft (fig. 3 *B, 2*). Six days later the skin sutures were removed. The tarsorrhaphy sutures were removed in twelve days. Six weeks later the lids were separated (fig. 3 *C*).

The pathologic diagnosis on examination of the excised portion of the lid was basal cell carcinoma. At the time of writing, twenty months later, the patient is doing well.

Case 4.—The patient presented an empty right socket with lagophthalmos, due to shortening of the upper and lower lids (fig. 4 *A*). The upper lid was considerably narrowed, and the lower lid, which had been reconstructed, was too thin and sagged from lack of support (fig. 4 *A* and *B*). At the time of repair, the right upper lid was first widened by means of a free whole skin graft taken from the left upper lid. Four weeks later a crescentic piece of preserved cartilage was fashioned. This was 1 cm. wide and 1 mm. thick; the vertical arm

measured 8 mm., and the horizontal arm, 18 mm. (fig. 4 *C*, dotted area). An incision was made about 10 mm. temporal to the outer canthus, the skin undermined, the cartilage plate slipped under the skin and the wound closed with two black silk sutures. Figure 4 *D* shows the lids in normal position, six weeks later.

*Repair of Defects Around the Socket.*—Bony defects around the orbit often give unsightly depressions and disturbances of contour which are disfiguring. If the defect is great, bone grafting should be done. In repair of the smaller defects, however, cartilage grafts suffice and are well adapted to this purpose. In 4 cases defects were repaired in this mannner, 2 of which are reported in detail.

CASE 5.—On admission the patient had an anophthalmic right orbit, cicatricial ectropia of the right upper and lower lids and loss of the upper fornix, due to cicatrices and synechias (fig. 5 *A*). He had an extensive defect of the right

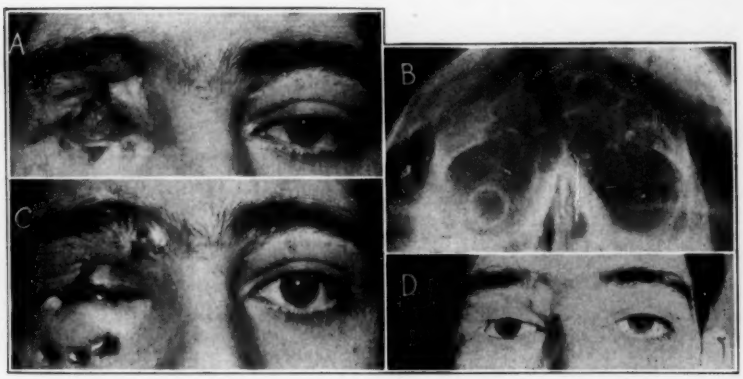



Fig. 5 (case 5).—*A*, appearance of the patient on admission. Note the depression under the medial half of the brow. *B*, roentgenogram of the skull, showing defect of the frontal bone. *C*, appearance immediately after repair of the depression with preserved cartilage. *D*, result eight weeks after operation. Note absence of depression.

frontal bone which followed operation for removal of multiple metallic foreign fragments (fig. 5 *B*). At the time of repair of the lid the wound in the upper lid was laid open widely and the bony defect filled in with a plate of preserved cartilage (fig. 5 *C*). The immediate result is shown in figure 5 *D*.

CASE 6.—The patient had a deep bony depression over the right zygoma (fig. 6 *B*), as well as an anophthalmic right socket and a medial notch of the right lower lid (fig. 6 *A*). The bony defect was repaired by laying open the soft tissues and fashioning an inlay of preserved cartilage cut to pattern. This cartilage plate was approximately 1 cm. thick at the deepest point. The wound was closed in layers, the muscle tissue with surgical gut and the skin with 0000 black silk sutures. The notch in the lid was repaired at the same time. Figure 6 *C* shows the result of repair five days later. The appearance five weeks later is shown in figure 6 *D*.

*Repairs of the Orbit.*—In 9 cases preserved cartilage was used in the orbit to fill out defects due to fractures. In 5 of these cases there was depression of the orbital floor and contents. In 1 of these cases the socket was anophthalmic, and the prosthesis required raising. In the other 4 cases there was ptosis of the globe. Two cases are reported in detail, with photographs.

In 4 cases preserved cartilage was used in an anophthalmic socket to fill in abnormally large cavities preceding reconstruction of the socket. In 2 of these cases a cartilage plate was used. In the other 2 cases chips of preserved cartilage were used to fill in large, cystlike, irregular spaces.

CASE 7.—On admission the patient presented ptosis of the left globe with enophthalmos, blepharoptosis and scarring of the tissues of the forehead, pulling his left brow up (fig. 7 *A*). He had fractures of the left portion of the frontal

Fig. 6 (case 6).—*A* and *B*, appearance of the patient on admission; *C*, appearance five days after repair of bony defect over the right zygoma with a preserved cartilage plate; *D*, final appearance five weeks later.

bone which extended into the posterior parietal region and the frontal ridge, with resultant depression and deformity of the left orbit (fig. 7 *B*). Vision was 20/20 in each eye; his chief complaint, of course, was diplopia. At operation, the lower orbital rim was exposed by an external incision, the periosteum of the orbital floor was lifted and a plate of preserved cartilage was inserted to elevate the eyeball. The wound was closed in layers. Figure 7 *C* shows the relative position of the eyes five days later, before removal of the sutures. Figure 7 *D* shows the patient thirteen days after operation. There was a residuum of 6 prism diopters of right hypertropia but no diplopia in the primary position.

CASE 8.—On admission, the patient had ptosis of the left globe with a deep depression above the eye as a result of sagging of the orbital contents. The eye was amblyopic (fig. 8 *A*). Repair was made exactly as in case 7. The result, ten days after operation, is shown in figure 8 *B*. Here, again, the disappearance of the supratarsal depression is to be noted.

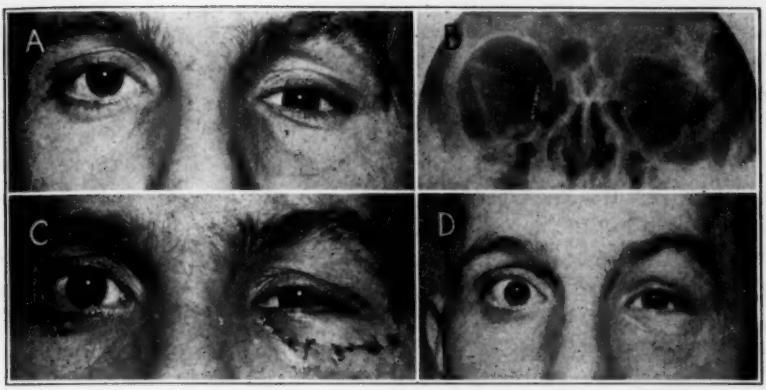



Fig. 7 (case 7).—*A*, ptosis and enophthalmos of the left globe; *B*, roentgenogram of the orbit seven months after injury; *C*, appearance five days after operation; *D*, result thirteen days after operation. Note that the eyes are on a level but that the enophthalmos and blepharoptosis persist. The depression beneath the left brow has disappeared.

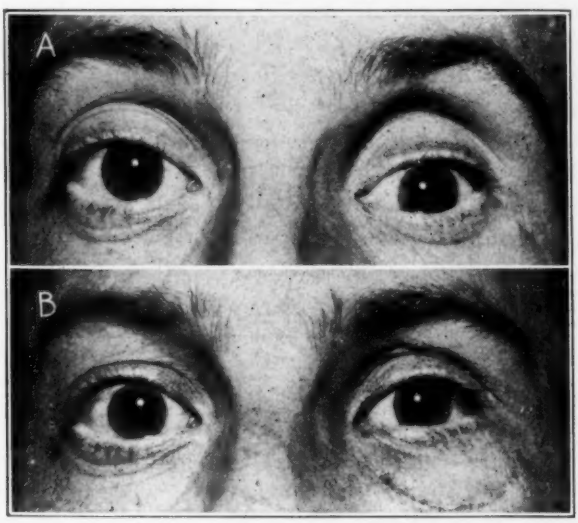



Fig. 8 (case 8).—*A*, ptosis of the left globe due to fracture of the orbital floor; *B*, result ten days after repair.

COMMENT

Preserved cartilage has been used most extensively, of course, by the plastic surgeon in reconstructions of the nose, ear, forehead, chin and other facial structures. This will probably always remain its greatest sphere of usefulness. But it can also be used effectively by the ophthalmic surgeon in reconstructions in and about the orbit, as reported.

Since preserved cartilage is a "dead" tissue, the question of what happens to it after grafting into the host is pertinent and germane. The most recent experimental study was carried out by Peer,[1] who studied the fate of living (autograft) and dead (isograft) human cartilage planted under the abdominal skin of human subjects. He found that fresh rib cartilage buried under the skin of its own human host survives for periods as long as six years and neither increases nor decreases in size. In the case of preserved human rib cartilage buried in other human hosts the grafts showed microscopic invasion by the surrounding host tissues and areas of absorption. There were also areas of calcification and early formation of bone. This process, however, was very slow, and "the bulk of the graft was still present two years after transplantation." So much for actual pathologic studies.

Clinically, Pierce and O'Connor[4] followed 182 cases for five years after using preserved cartilage grafts and stated that they prefer them to autografts. O'Connor[5] followed 375 cases with isografts of cartilage and found that the grafts had retained their original size and identity in all but 7 cases. Only 1 graft was completely lost, owing to infection. In my series, 2 patients were followed for eighteen months; 3 were seen after twelve months, and the rest were followed for at least six months. No visible or palpable change in the grafts was noted. There were no infections.

It seems to me that the ultimate histologic fate of the cartilage isograft is of less import to the ophthalmic surgeon than to the plastic surgeon. If absorption of a graft used to reshape a nose or chin occurs, the result may be failure, with further surgical repair necessary. On the other hand, assuming that a thin plate of preserved cartilage implanted into a lid, for instance, is ultimately completely absorbed and converted into dense fibrous tissue, such a change, according to all available evidence, would not occur for several years, if at all. Furthermore, the resultant tissue structure is not unlike that of the tarsal "cartilage," which furnishes ample support to the lid. The object of the surgical procedure has been accomplished in any case. The use of the isograft, moreover, has obviated the necessity of taking cartilage from the patient's ear or rib, or tarsus from another lid, and has simplified and shortened the operation for both surgeon and patient.

Spaeth [6] stated that "cartilage and corneal tissues are perhaps the only grafts which can be used with success as an isograft. All other grafts are likely to result in failures unless they are homografts." Recent reports seem to show that the field of usefulness of isografts may not be so narrow. Thus, Filatov [7] and his school have done successful grafting with refrigerated tissues. Recently Rosen [8] reported a successful transfer of the conjunctiva from a cadaver. The tremendous need for restorative surgery resulting from the recent war has stimulated much work and experimentation in this field and has furnished ophthalmic surgeons with an unparalleled opportunity to learn and profit from it. It may be that as a result of this work the whole field of isografting and heterografting will have to be reevaluated. There is no reason that more opthalmic surgeons should not take a hand in this work.

Certainly, in selected cases I can think of no important objections to the use of cartilage isografts in plastic surgery of the eye. I can see several valid reasons for its use. I hope more oculists will try it and report their results.

## SUMMARY AND CONCLUSIONS

Seventeen cases are reported in which preserved cartilage was used as an isograft. In 4 cases it was used in reconstruction of the lid to replace lost tarsal "cartilage." In another 4 cases it was used to repair bony depressions outside the orbit. In 9 cases preserved cartilage was used inside the orbit to repair depressions of the floor and walls due to fractures. The results were good.

The advantages of using preserved cartilage in reconstruction of the lids and the socket are enumerated.

In selected cases there seems to be no contraindication to the use of preserved cartilage in plastic surgery of the eye.

Mr. Herbert M. Krauss made the drawings illustrating the technic of the various operative procedures.

63 East Seventy-Five Street.

6. Spaeth, E. B.: The Principles and Practice of Ophthalmic Surgery, Philadelphia, Lea & Febiger, 1944, p. 88.

7. Filatov, V. P.: Tissue Therapy in Ophthalmology, Am. Rev. Soviet Med. **2**:53-66, 1944.

8. Rosen, E.: Heterogeneous Conjunctival Transplantation, Am. J. Ophth. **29**:193-195, 1946.

# PENETRATION OF LOCALLY APPLIED BAL INTO THE ANTERIOR CHAMBER OF THE RABBIT EYE

IRVING H. LEOPOLD, M.D.
AND
WILLARD H. STEELE, M.D.
PHILADELPHIA

WHEN it was found that the use of BAL (2,3-dimercaptopropanol) was of considerable value, both prophylactically and therapeutically, in the treatment of eyes exposed to lewisite (2-chlorobetachlororinylarsine) burns,[1] the problem arose as to what extent BAL penetrated through the normal or the abnormal cornea and into the anterior chamber. Since BAL essentially neutralizes the toxic heavy metal arsenic in lewisite burns, the possibility that BAL might be of importance in treatment of intoxications due to other metals, such as lead, mercury and cadmium, also warranted this study.

An accurate, yet practical, method for the quantitative estimation of BAL was investigated. The cobalt nitrate test of Kensler and Rhoads,[2] the porphyrindin test of Greenstein[3] and the iodometric titration of sulfhydryl groups, as used by Woodward and Fry for glutathione, were tried. The iodometric titration was chosen and used exactly as recommended by Woodward and Fry,[4] except that instead of a 0.001 normal solution of potassium iodate we employed a 0.0005 normal solution of potassium iodate. Because of the extreme dilution of this reagent, it was necessary to check on the accuracy of the method by titrating it against a known dilute solution of BAL to determine whether the method could actually be employed for this compound.

Table 1 shows the values for the sulfhydryl groups obtained, expressed in cubic centimeters of 0.0005 normal potassium iodate, when

---

From the Department of Ophthalmology of the University of Pennsylvania Hospital.

The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the office of Scientific Research and Development and the University of Pennsylvania.

1. Personal communications to the authors: Stocken, L. A., and Thompson, R. H. S. (1941). Mann, I.; Pirie, A., and Pullinger (1941). Clark, A. J.; Robson, J. H., and Scott, G. I. (1941). Adler, F. H.; Leopold, I. H.; Crandall, A. S., and Steele, W. H. (1942). Hughes (1942).

2. Kensler, C. J., and Rhoads, C. P.: Personal communication.

3. Greenstein, J.: J. Biol. Chem. **125**:501, 1938.

4. Woodward, G. E., and Fry, E. G.: J. Biol. Chem. **97**:465, 1932.

the solution was titrated against aqueous solutions of BAL containing 0.04, 0.06, 0.1, 0.16 and 0.2 mg., respectively, per cubic centimeter. The table also includes figures for the same concentrations of BAL in ethylene glycol and for ethylene glycol alone. From these figures, a graph has been plotted showing that practically a straight line is obtained, which corresponds with the straight line prepared from calculated theoretic values (graph). The difference between the actual readings and the theoretic ones may be explained on the basis of the purity of the sample used and on errors in technic, which for these

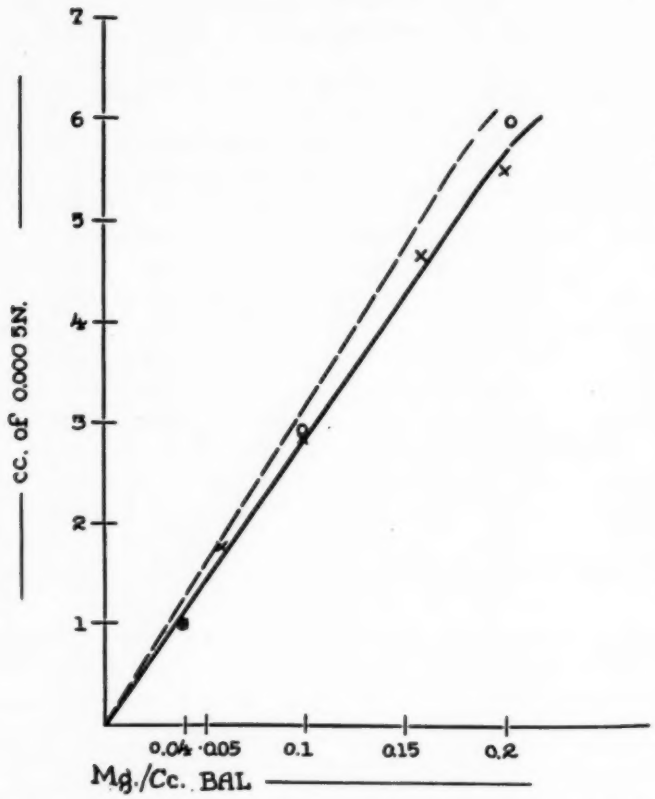
TABLE 1.—*Standardization of 0.0005 Normal Solution of Potassium Iodate Used in Titration of BAL*

| | Concentration of BAL, Mg./Cc. | | | | | |
|---|---|---|---|---|---|---|
| Aqueous solution | 0.00 | 0.04 | 0.06 | 0.1 | 0.16 | 0.2 |
| | Readings in Cc. of 0.0005/N Potassium Iodate | | | | | |
| | 0.13 | 1.17 | 1.88 | 3.10 | 5.035 | 5.61 |
| | 0.11 | 1.16 | 1.90 | 3.10 | 4.906 | 5.70 |
| | 0.12 | 1.17 | 1.98 | 2.98 | 4.820 | 5.45 |
| | 0.14 | 1.18 | 1.95 | 2.99 | 4.755 | 5.75 |
| | 0.11 | 1.15 | | 3.00 | 4.70 | 5.70 |
| | | 1.14 | | 3.01 | 4.665 | 5.51 |
| | | 1.12 | | 3.00 | | 5.61 |
| | | 1.11 | | 3.00 | | 5.60 |
| | | | | 2.97 | | 5.59 |
| | | | | 2.99 | | 5.55 |
| | | | | 3.10 | | |
| Average value | 0.12 | 1.13 | 1.92 | 3.02 | 4.813 | 5.607 |
| Average range | ±0.02 | ±0.04 | ±0.06 | ±0.08 | ±0.148 | ±0.15 |
| Ethylene glycol solution | 0.20 | 1.310 | | 3.19 | | 6.10 |
| | 0.22 | 1.275 | | 3.185 | | 6.13 |
| | | 1.300 | | 3.17 | | 6.30 |
| | | 1.295 | | | | |
| Average value | 0.21 | 1.295 | | 3.181 | | 6.17 |
| Average range | ±0.02 | ±0.02 | | ±0.01 | | ±0.13 |

titrations were never greater than 5 per cent, and in the majority of readings were less than 3 per cent.

Using this method for determination of BAL, a dilute solution containing 10 mg. of BAL in 50 cc. of water was prepared, and various concentrations of this solution were titrated at varying time intervals. The data from these experiments are included in table 2. These results indicate that there is a definite loss of sulfhydryl groups when BAL is dissolved in a dilute aqueous solution and allowed to stand. This loss is practically complete within forty-eight hours. When BAL is dissolved in ethylene glycol in the same concentration, as the findings on table 2 indicate, there is practically no loss in forty-eight hours. If a 1 per cent aqueous solution is tested after ten days, deterioration can be noted, but it is slight.

Before this test could be used for determination of the degree of penetration of BAL, it was necessary to determine the amounts of solution of potassium iodate required to react with the sulfhydryl-bearing compounds of normal aqueous humor. The 12 eyes of 6 rabbits were used for this test, and the values are recorded in table 3. It can be seen that the greatest range for values of normal aqueous




Comparison of the theoretic and obtained values for BAL by the iodometric titration method. In this graph, crosses indicate values for aqueous solution; circles, values for solutions in ethylene glycol; the broken line, theoretic values for 100 per cent pure BAL, and the solid line, values actually obtained for BAL in aqueous solution and in solution in ethylene glycol.

humor were from 3.98 to 8.5 cc. of 0.0005 normal solution of potassium iodate for each cubic centimeter of aqueous humor, but that the difference between the two eyes of the same rabbit was never greater than 0.42 cc. of 0.0005 normal solution of potassium iodate for each cubic centimeter of aqueous humor. As the data in table 3 indicate,

the previous use of 2 drops of 2 per cent ethyl morphine hydrochloride failed to increase the values obtained. It made no significant difference in the values obtained with normal aqueous humor whether or

TABLE 2.—*Loss of Sulfhydryl Groups* in Dilute Aqueous Solution of BAL Compared with Loss in Dilute Solutions of BAL in Ethylene Glycol**

| Aqueous Solution, Mg./Cc. | | | Solution in Ethylene Glycol, Mg./Cc. | | |
|---|---|---|---|---|---|
| 0.04 | 0.1 | 0.2 | 0.04 | 0.1 | 0.2 |
| 0.0005/N Potassium Iodate, Cc. | | | 0.0005/N Potassium Iodate, Cc. | | |
| 1.13 | 3.02 | 5.60 | 1.295 | 3.18 | 6.17 |
| | 1 Hour Later | | | | |
| 1.06 | 2.75 | 5.38 | | | |
| | 2 Hours Later | | | | |
| 0.946 | 2.68 | 5.23 | | | |
| | 24 Hours Later | | | 24 Hours Later | |
| 0.78 | 2.30 | .... | 1.30 | 3.05 | 6.20 |
| | 30 Hours Later | | | | |
| 0.25 | 0.35 | 0.54 | | | |
| | 48 Hours Later | | | 48 Hours Later | |
| 0.12 | 0.15 | .... | 1.25 | .... | 6.15 |

* Values for the sulfhydryl group are expressed in terms of cubic centimeters of 0.0005 normal solution of potassium iodate. Each recorded value is an average of at least five readings, all falling within a 3 per cent error.

TABLE 3.—*Values for Sulfhydryl Groups for Normal and for Secondary Aqueous**

| | Cc. | | Cc. | | Cc. |
|---|---|---|---|---|---|
| Rabbit 142 | | Rabbit 142 (1 hr. later) | | Rabbit 115 (long standing mustard gas burn with keratitis) | |
| O. D. | 4.40 | O. D. | 10.60 | O. D. | 6.325 |
| O. S. | 3.98 | O. S. | 10.42 | O. S. | 5.30 |
| Rabbit 143 | | Rabbit 143 (1 hr. later) | | | |
| O. D. | 5.24† | O. D. | 11.10 | | |
| O. S. | 5.50† | O. S. | 13.80 | | |
| Rabbit 145 | | | | | |
| O. D. | 5.5 ‡ | | | | |
| O. S. | 5.1 ‡ | | | | |
| Rabbit 146 | | | | | |
| O. D. | 4.98 | | | | |
| O. S. | 5.00 | | | | |
| Rabbit 147 | | | | | |
| O. D. | 8.5 | | | | |
| O. S. | 8.1 | | | | |
| Rabbit 148 | | | | | |
| O. D. | 7.68 | | | | |
| O. S. | 7.35 | | | | |

* Values are expressed in cubic centimeters of 0.0005 normal potassium iodate required for each cubic centimeter of aqueous. The greatest range from one animal to another is 3.98 to 8.5 cc. The greatest range in any one animal between the right and the left eye is 0.42 cc.

† Eyes received 2 drops of 2 per cent ethyl morphine hydrochloride before puncture of the aqueous.

‡ Proteins precipitated with sulfosolicylic acid.

not the proteins were precipitated before titration. However, when secondary aqueous was titrated without precipitating the proteins, there was a definite increase in the number of cubic centimeters of the

solution of potassium iodate required per cubic centimeter of aqueous humor. These figures are also included in table 3. An animal in which chronic keratitis had been induced with mustard gas (2-chloroethylsulfide) failed to show concentrations in the aqueous humor above those obtained for normal eyes. The probable substances in the aqueous humor which give titration values with this test are ascorbic acid, glutathione and cysteine. With the foregoing data, studies of the penetration of BAL into the aqueous humor of normal rabbit eyes were then undertaken.

Five per cent BAL in water was applied to the conjunctival cul-de-sac of 3 rabbits. Five minutes after the application of 4 drops of

TABLE 4.—*Penetration of Solutions of BAL in Water and in Ethylene Glycol into the Anterior Chamber**

| | Time of Limbal Puncture After Application | | | | | |
|---|---|---|---|---|---|---|
| | 5 Minutes | | 15 Minutes | | 30 Minutes | |
| | Rabbit 136 | Cc. | Rabbit 142 | Cc. | Rabbit 139 | Cc. |
| 5% BAL in water (in both eyes) | O. D..... | 21.23 | O. D..... | 11.15 | O. D..... | 11.00 |
| | O. S..... | 19.40 | O. S..... | 13.00 | O. S..... | 10.40 |
| | Rabbit 137 | | Rabbit 138 | | Rabbit 150 | |
| | O. D..... | 18.85 | O. D..... | 13.07 | O. D..... | 5.92 |
| | O. S..... | 21.60 | O. S..... | 10.00 | O. S..... | 8.00 |
| | Rabbit 140 | | | | | |
| | O. D..... | 25.00 | | | | |
| | O. S..... | 7.81 | | | | |
| 5% BAL in ethylene glycol (in both eyes) | Rabbit 152 | | Rabbit 157 | | Rabbit 151 | |
| | O. D..... | 14.15 | O. D..... | 4.56 | O. D..... | 5.90 |
| | O. S..... | Lost | O. S..... | 5.08 | O. S..... | 5.80 |
| | Rabbit 154 | | | | Rabbit 153 | |
| | O. D..... | 8.37 | | | O. D..... | 9.45 |
| | O. S..... | 7.41 | | | O. S..... | 10.10 |
| | Rabbit 158 | | | | Rabbit 156 | |
| | O. D..... | 10.85 | | | O. D..... | 8.80 |
| | O. S..... | 6.53 | | | O. S..... | 7.52 |

* Values are expressed in cubic centimeters of 0.0005 normal potassium iodate per cubic centimeter of aqueous.

this solution, the eyes were thoroughly irrigated with isotonic solution of sodium chloride, and punctures into the anterior chamber made, with the rabbit under ether anesthesia; titrations were made immediately on these samples of aqueous humor. With the same method, 4 drops of 5 per cent BAL in ethylene glycol were placed in the conjunctival cul-de-sac, and the amount of the drug in the aqueous humor was evaluated. In other rabbits, the penetration of BAL into the anterior chamber after fifteen and thirty minutes was similarly determined. The results of these studies are presented in table 4. It is evident that the concentration of BAL in the anterior chamber was greater when water was used as a vehicle than when ethylene glycol was used.

Because it has been shown that the range for normal aqueous humor varies from 3.98 to 8.5 cc. of 0.0005 normal solution of potassium iodate per cubic centimeter of aqueous humor, it might be argued that the figures in table 4 may represent not the actual difference in the degree of penetration of BAL in aqueous solution as compared with that in solution in ethylene glycol, but only the variations to be found in normal aqueous humor. However, it has been shown that the range of variations for normal aqueous humor between the two eyes of the

TABLE 5.—*Penetration of BAL in Aqueous, Ethylene Glycol and Ointment Vehicles*

| | Time of Limbal Puncture After Application | | | |
|---|---|---|---|---|
| | 5 Minutes | | 30 Minutes | |
| Water and ethylene glycol * | Rabbit 162 | Cc. | Rabbit 161 | Cc. |
| | O. D. | 17.70 | O. D. | 17.17 |
| | O. S. | 9.24 | O. S. | 7.77 |
| | Rabbit 163 | | Rabbit 164 | |
| | O. D. | 20.83 | O. D. | 5.99 |
| | O. S. | 14.52 | O. S. | 5.50 |
| | Rabbit 168 | | | |
| | O. D. | 27.6 | | |
| | O. S. | 6.7 | | |
| | Rabbit 171 | | | |
| | O. D. | 14.65 | | |
| | O. S. | 9.55 | | |
| | Rabbit 172 | | | |
| | O. D. | 12.25 | | |
| | O. S. | 9.55 | | |
| K-Y jelly and Friedenwald (Fuqua)† | Rabbit 160 | | Rabbit 155 | |
| | O. D. | 12.81 | O. D. | 7.40 |
| | O. S. | 6.08 | O. S. | 6.15 |
| | Rabbit 165 | | Rabbit 159 | |
| | O. D. | 15.22 | O. D. | 4.65 |
| | O. S. | 10.03 | O. S. | 4.60 |
| | Rabbit 169 | | | |
| | O. D. | 11.26 | | |
| | D. S. | 7.60 | | |

* The right eye received 5 per cent BAL in aqueous solution, and the left eye, 5 per cent BAL in solution of ethylene glycol.

† The right eye received 5 per cent BAL in K-Y jelly, and the left eye, 5 per cent BAL in modified Friedenwald-Fuqua ointment.[5]

same rabbit is always less than 0.4 cc. of 0.0005 normal solution of potassium iodate; so 4 drops of a 5 per cent solution of BAL in water were placed in the right eye of 5 rabbits and 4 drops of a 5 per cent solution of BAL in ethylene glycol were placed in the left eyes of the same rabbits. Punctures into the anterior chamber were made five minutes later, and titrations made immediately; the values are recorded in table 5. It can be seen that the solution of BAL in water gave consistently higher concentrations of BAL in the aqueous humor than the solution in ethylene glycol.

The concentrations of BAL in the anterior chamber thirty minutes after instilling the preparations in water and in ethylene glycol showed

no significant difference in penetration of the two solutions. These data are included in tables 4 and 5.

Penetration of 5 per cent BAL in ointment was also tested. Five per cent BAL in K-Y lubricating jelly N. N. R. was placed in the right eyes and the same quantity of 5 per cent BAL in a modified Friedenwald (Fuqua) ointment [5] in the left eyes of 3 rabbits. The cul-de-sacs were thoroughly irrigated with isotonic solution of sodium chloride after five minutes and punctures into the anterior chamber made. Titrations done immediately showed that high concentrations of BAL in the aqueous humor were obtained when K-Y jelly was the vehicle. When these titrations were made thirty minutes after applying BAL in the ointment bases, no significant difference could be demonstrated between the values for the two ointments.

## COMMENT

It is evident from these data that solutions of BAL in water and in ethylene glycol penetrate through the cornea into the anterior chamber. The penetration from a water vehicle was more rapid than that from an ethylene glycol vehicle. Likewise, a water-containing ointment allowed greater penetration than did a nonaqueous base. However, aqueous solutions of BAL are unstable, and for the majority of practical uses the stability of the preparation will be more important than the rate of penetration.

## CONCLUSIONS

1. Aqueous solutions of BAL (2,3-dimercaptopropanol) deteriorate more rapidly than solutions in ethylene glycol, at least so far as sulfhydryl groups are concerned, and the more dilute the aqueous solutions of BAL the more apparent the loss.

2. Greater penetration into the aqueous humor occurs from the use of a 5 per cent solution of BAL in water than from the use of a 5 per cent solution of BAL in ethylene glycol.

3. BAL penetrates more readily from a water-containing base, such as K-Y jelly, than it does from a nonaqueous base, such as Friedenwald-Fuqua ointment.

Hospital of the University of Pennsylvania (4).

5. The modified Friedenwald-Fuqua ointment contains peanut oil, 36.95 per cent; wool fat, 8 per cent; cetyl alcohol, 10 per cent; glyceryl monostearate, 10 per cent; white petrolatum, soft, 25 per cent; benzyl benzoate, 5 per cent; mixed tocopherols, 0.05 per cent, and medicament, 5 per cent.

# ATROPHY OF THE OPTIC NERVE ASSOCIATED WITH TABES DORSALIS AND WITH GLAUCOMA

LEO HESS, M.D.
BOSTON

IN A SMALL percentage of cases of tabes dorsalis, about 15 per cent according to Uhthoff,[1] bilateral progressive atrophy of the optic nerve can be detected by the pronounced pallor of the optic disk. It is an early sign, preceding all other manifestations of tabes, even the subjective disorder of vision. Its salient feature is the atrophy of the nerve head, without any noticeable change in the arteries. It is to be differentiated from another, similar, type of atrophy, in which in addition to the discoloration of the papilla the arteries are narrowed, owing to an inflammatory process involving both the arterial wall and the surrounding tissue. Whereas in the latter type of atrophy syphilis of the meninges is suggested as the underlying cause, the pathogenesis of the first type is obscure. From the clinical point of view, it is worth while to note the slow but relentless progress of visual disturbances; the constant bilaterality; the early reduction of color appreciation (for red and green); the early failure of vision to adapt itself to the dark; the lack of involvement of any of the cranial nerves, such as is frequently seen in cases of syphilitic basilar meningitis; the presence of the syphilitic infection many years before the atrophy of the optic nerve, and the classic Argyll Robertson sign. Later, absolute fixity of the pupils may occur. The pupils, sometimes anisocoric, are miotic—in juvenile tabes often mydriatic. Their response to atropine, according to my personal experience, is slow. Ectopia of the pupils is rare. In the majority of cases a progressive peripheral contraction of the visual fields takes place, central vision being spared for a long time. Occasionally, however, central scotoma or binasal or temporal, or even bitemporal, hemianopsia has been recorded. The hemianopsia reminds one of the well known visual defects found with disorders of the pituitary gland. Complicating syphilis of the meninges in the region of the chiasm may play a role of importance in some instances. Oliver,[2] in his statistical studies, found that 90 per cent of the cases of tabetic atrophy of the

1. Uhthoff, W., in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, W. Engelmann, 1911, vol. 11, chap. 22.

2. Oliver, C. A.: Am. J. M. Sc. **120**:49, 1900.

optic nerve were encountered in males. The course of the tabes in cases of amaurosis is surprisingly mild ("Benedikt's [3] law").

As the basis of the condition there is undoubtedly an anatomic lesion of the optic pathways, involving in later stages the entire diameter of the optic nerve, the axons as well as the myelin sheaths. The primary site and the nature of this lesion are still *sub judice*. The pathologic observations recorded in the literature are confusing. Léri [4] failed to observe any changes in the ganglionic layer of the retina, although almost every normal fiber in the optic nerve had disappeared. Degenerative alterations of the optic tract in the region of the lateral geniculate body could not be demonstrated by Léri,[4] Moeli [5] or Holden.[6] In an inflammatory parenchymatous process of the optic nerve, secondary degeneration of the ganglion cells of the retina or of the external geniculate body is to be expected. Stargardt [7] expressed the belief that there might occasionally be neurotic degeneration in the optic tracts or in the corpus geniculatum laterale. His conclusions, however, are not convincing, since in most of his cases the eyegrounds were normal. In recent yeears in 4 cases of complete bilateral blindness associated with tabes Deutsch [8] observed atrophy of certain components of the corpus geniculatum laterale, whereas the geniculocortical neurons were intact. These observations were confirmed by Hechst.[9] One might, therefore, be justified in suggesting that atrophy of the optic nerve begins behind the bulbus, somewhere in the optic pathways, producing secondary degeneration along the optic nerve and the optic tract as far as, and including, the lateral geniculate body. Gudden's commissure (Moxter [10]), a structure which, according to modern anatomists, does not belong to the central optic system, has been noted to be intact; furthermore, the so-called residual bundle of the *bandelette* of Marie and Léri [11] (*faisceau residuaire de la bandelette*), belonging to the optic tract, is not involved. The conclusion is to be drawn that the anatomic alteration is located within the diencephalon (or, better, in the posterior part of the diencephalon) and is primarily confined to a certain group of fibers of the

3. Benedikt, M.: Wien. med. Presse **22**:1, 40, 101 and 135, 1881.

4. Léri, A.: Nouv. iconog. de la Salpêtrière **17**:304, 1904.

5. Moeli, C.: Arch. f. Psychiat. **30**:907, 1898; cited by Wilson, K.: Neurology, edited by A. N. Bruce, Baltimore, Williams & Wilkins Company, 1940, vol. 1, p. 484.

6. Holden, T.: Arch. f. Ophth. **38**:110, 1899; cited by Wilson, S. A. K., in Neurology, edited by A. N. Bruce, Baltimore, Williams & Wilkins Company, 1940, vol. 1, p. 484.

7. Stargardt, K.: Arch. f. Psychiat. **51**:711, 1913.

8. Deutsch, H.: Arb. a. d. neurol. Inst. a. d. Wien. Univ. **31**:129, 1929.

9. Hechst, B.: Arch. f. Psychiat. **95**:107, 1931.

10. Moxter: Ztschr. f. klin. Med. **29**:334, 1896.

11. Marie, P., and Léri, A.: Rev. neurol. **13**:246, 1905.

optic tract—in other words, it is a "systemic" alteration of nerve fibers within the optic tract, including certain components of the corpus geniculatum laterale. According to the literature and to personal clinical experience, the papillomacular bundle appears to be spared, or to be involved only in the later stages. There are several good reasons for believing that this bundle, arising from ganglion cells of the macula and the paramacula, represents in itself an entity, which primarily is not involved in the "tabetic" process. The nature of this "systemic" lesion is not clear. It may not be inflammatory, since, as has been mentioned, there is no evidence of degeneration of the ganglion cells of the retina. The cornea and the choroid likewise are not inflamed. The lesion is neither ascending nor exogenous (toxic). There are no signs of increased local pressure. One might compare this lesion to the systemic lesions observed in many congenital diseases of the spinal cord (such as Friedreich's disease and amyotrophic lateral sclerosis) or to the spinal lesions of acquired and "inherited" tabes dorsalis. In tabes dorsalis only certain fibers of the posterior columns and, specifically, the central part of the posterior roots are affected, i. e., that part where the root, before entering the spinal columns, takes on a "central" character. The same selective alteration of certain fibers is the significant feature of tabetic atrophy of the optic nerve. It is probable, although it has not been conclusively proved, that this type of bilateral atrophy of the optic nerve (without neuritic signs) may occur not only in the tabes of adults and of children with congenital syphilis, but in another hereditary syphilitic condition of the spinal cord, namely, combined systemic degeneration.

The lesion under discussion is not "syphilitic" *sensu strictissimo,* since spirochetes have never been demonstrated within the optic nerve fibers. It is interesting, furthermore, that although in cases of dementia paralytica spirochetes are numerous in the brain, atrophy of the optic nerve is rare. Antisyphilitic treatment (both specific and nonspecific) does not exert any great influence on the course of atrophy of the optic nerve. The atrophy is progressive, even though the blood and spinal fluid have become serologically "negative." In reviewing the clinical material in the General Hospital of Vienna from 1905 to 1925, John [12] found that despite the progress of antisyphilitic treatment the percentage of cases of tabetic atrophy of the optic nerve remained unchanged. This fact, together with the predominance in males, as shown by Oliver's [2] statistics, and the rarity of atrophy of the optic nerve in dementia paralytica, as compared with its incidence, 15 per cent, in tabes would indicate that an endogenous factor may be decisive in the pathogenesis. I shall return to this point again.

12. John, I.: Ztschr. f. Augenh. **69**:283, 1929.

The bilateral character of the lesion is certainly indicative of a central, and not a peripheral, origin. The systemic, noninflammatory, nontoxic, nonascending, central process may likewise lead one to suggest with due caution that its background is a congenital anomaly. The optic nerve not being a "peripheral" nerve, but in point of development and structure, a central nerve tract (fasciculus opticus), the concept of tabetic atrophy of the optic nerve as a systemic degeneration may meet with no great opposition. In view of the fact that in cases of tabes dorsalis the spinal cord exhibits infantile proportions and the arrangement of the spinal tracts is variable, often differing from the normal, regular, pattern (Stern [13]), it is fair to assume that an analogous irregularity in the structure of the optic nerve and optic tract may account for the variety of the visual defects associated with tabetic atrophy of the optic nerve. Because of this variability in visual disturbance, apparently, it has been found hard to correlate the anatomic and the clinical features.

Originally the lesion may be confined to a small part of the brain, i. e., the posterior section of the diencephalon, from which are derived not only the lateral geniculate bodies, but also the optic tracts and nerves, the neural part of the hypophysis and the epiphysis. The important vegetative center (Karplus and Kreidl [14]; Ranson [15]) is located not far away. The diencephalon is the area where the primary site of a certain type of primary atrophy of the optic nerve is assumed to exist (Hess [16]) —the type associated with adiposity and genital disorders. It has been pointed out, on the other hand, that normal physical growth is closely related to the activity of a normal brain and of a normal hypophysis and epiphysis (Hess [16]). The location of the congenital anomaly would lead one to expect some abnormality in the physical growth of persons with atrophy of the optic nerve. Syphilis is the precipitating, not the causative, agent. In support of this concept, it is essential to provide evidence, (*a*) that tabes dorsalis is not merely a disease of the spinal cord but may involve the diencephalon in a certain percentage of cases, as does Friedreich's disease (Hess [16]), and (*b*) that definite characteristics of body build and physical growth are clinically noticeable in tabetic persons with atrophy of the optic nerve, demonstrating an endogenous alteration of the diencephalic area.

---

13. Stern, R.: (*a*) Arb. a. d. neurol. Inst. a. d. Wien. Univ. **14**:329, 1908; (*b*) Ueber körperliche Kennzeichen der Disposition zur Tabes, Leipzig, F. Deuticke, 1912.

14. Karplus, P., and Kreidl, A.: Arch. f. d. ges. Physiol. **129**:138, 1909; **135**:401, 1910; **143**:119, 1911; **171**:192, 1918.

15. Ranson, S. W., in Harvey Lectures, Baltimore, Williams & Wilkins Company, 1936.

16. Hess, L.: Pathogenesis of Glaucoma and "Glaucomatous" Atrophy of the Optic Nerve, Arch. Ophth. **37**:324 (March) 1947.

DIENCEPHALIC SIGNS ASSOCIATED WITH TABES DORSALIS

Signs of diencephalic involvement associated with tabes dorsalis have been reported by many authors. Guillain [17] noted athetoid movements, clonism, tic and rhythmic tremor, confined particularly to the facial musculature and to the velum palatinum, and in other instances to the muscles of the fingers ("tabetic athetosis"). Schilder and Stengel [18] gave evidence of an anatomic lesion of the great basal ganglions in a case of tabes with severe ataxia and alteration of the *Stellfunction,* without sensory defects in the arms but with slow athetoid movements of both legs. Dereux [19] expressed the belief that signs of derangement in function of the infundibulum—adiposity, loss of hair, sexual disorders and narcolepsy—may be encountered in tabetic patients. In line with this statement is the coincidental occurrence of tabes and lipomatosis (Weiss [20]), since in some cases of lipomatosis (Dercum [21] and many other authors) anatomic changes in the hypophysis, an important part of the hypothalamus, have been observed. More important, and, as will soon be seen, of fundamental significance, is Dercum's observation on a tabetic patient with signs of acromegaly, due to enlargement of the glandular part of the hypophysis, as proved by autopsy. It is recognized that acromegaly may not seldom be associated with tabes. Dercum reported sclerosis of the posterior columns in his case; Buday and Jancso [22] and Arnold [23] observed degeneration of Goll's column in cases of acromegaly; Tamburini [24] noted degeneration of Burdach's funiculus, and Bonardi,[24] degeneration of the posterior and lateral columns, in other cases of this disorder. The clinical course of the tabes in most of these cases was mild. Not only the full blown picture of tabes but the rudimentary signs, such as loss of the knee jerk, lightning pains and disturbances of the bladder, have been noticed in association with acromegaly ("pseudotabes pituitaria"). It is not impossible that in some of these cases the tabes was extremely mild or was early arrested. Not merely acromegaly, but occasionally another diencephalic disorder—underdevelopment of the pituitary body with dwarfism—is to be found combined with tabes dorsalis, the course of which, again, is mild, or even asymptomatic. In a case recorded and published by Katzenstein,[25] that of a woman aged 51, dwarfism, tabes with atrophy of the optic nerve and retinitis pigmentosa

17. Guillain, G.: Neurol. Centralbl. **47**:74, 1927.
18. Schilder, P., and Stengel, E.: Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:613, 1928.
19. Dereux, I.: Neurol. Centralbl., 1902, p. 404.
20. Weiss, I.: Verhandl. d. deutsch. Gesellsch. f. inn. Med., Feb. 9, 1905.
21. Dercum, F.: J. Nerv. & Ment. Dis. **35**:507, 1908.
22. Buday, K., and Jancso, N.: Deutsches Arch. f. klin. Med. **60**:385, 1898.
23. Arnold, T.: Virchows Arch. f. path. Anat. **135**:1, 1894.
24. Cited by Stern.[13b]
25. Katzenstein, R.: Virchows Arch. f. path. Anat. **289**:222, 1933.

were present. Her height was 131 cm.; her weight, 127.6 Kg., and the circumference of the skull, 50.5 cm. She had never menstruated. The labia majora were small and the labia minora hardly recognizable; the trunk and axillas were hairless; the nipples were undeveloped. The abdominal wall and the thighs were fat. The uterus and the clitoris were very small; the ovaries were the size of a half-bean; the hypophysis was the size of a lentil; the anterior lobe was almost entirely replaced by fibrous tissue. There was a gray degeneration of the posterior columns throughout the length of the spinal cord. Bilateral atrophy of the optic nerve and retinitis pigmentosa with progressive impairment of vision had been present since the thirtieth year. There was no ataxia of the hands. Romberg's sign was positive. Hammer toe was present bilaterally. The mother had had 16 children and 2 abortions. The case deserves attention because of the coincidence of atrophy of the optic nerve, genital disorders and adiposity, a syndrome to which attention has previously been directed (Hess [16]). The course of the tabes was mild, almost asymptomatic, with involvement of the pituitary body. The case reminds one of Benedikt's law and suggests that the unusually mild course of the disease in certain cases of tabes with atrophy of the optic nerve may be related to an alteration of the diencephalic-hypophysial system. Noteworthy is the fertility of the patient's mother. This is in line with Nettleship's [26] observations; he reported an average of 9 children to each family tainted with retinitis pigmentosa. The tabes dorsalis and the retinitis pigmentosa in Katzenstein's case were congenital. The same may be true, although it has not been proved, for atrophy of the optic nerve, or at least for the anlage. In a case of pituitary dwarfism with hypoplasia of both optic nerves reported by Kraus,[27] the syndrome of adiposity, genital disorders (hypoplasia of the external genital organs and cystic degeneration of both ovaries), malformation of the pituitary body and extensive alteration of the optic nerve could again be demonstrated.

From the clinical viewpoint, the loss of libido sexualis and voluptas in the early states of tabes dorsalis and the sterility of tabetic women (from 50 to 60 per cent are childless), on the one hand, and the satyriasis and priapism, occasionally lasting for weeks, on the other, point to a lesion of the diencephalon. According to my personal experience, an initial loss of weight represents a first sign of tabes. This "unexplained" loss of weight may be due to damage to the vegetative center. But there are also tabetic patients in good physical condition, with rosy cheeks and well developed panniculus adiposus—these are the patients with atrophy of the optic nerve!

26. Nettleship, J.: Tr. Ophth. Soc. U. Kingdom **7**:301, 1887; **29**:128, 1909.
27. Kraus, E. I.: Beitr. z. path. Anat. u. z. allg. Path. **65**:535, 1919.

In epidemic encephalitis, with its predilection for the mesencephalon and the diencephalon, tabetiform signs (loss of weight, the Argyll Robertson sign or absolute fixity of the pupils, abolition of the tendon reflexes, hypotonia of the muscles and a neuritic (?) lesion of the optic nerves) are well known. In this connection, the association of tabes with another organic disease of the mesencephalon and diencephalon—paralysis agitans—is noteworthy.

The conclusion seems justified that with tabes dorsalis anatomic or functional disorders of the diencephalon are not uncommon. A primary alteration of the hypophysis, evidenced by signs of acromegaly, may, on the other hand, occasionally present signs of mild, arrested tabes. The diencephalic disorder is acquired or congenital, but even when acquired may be connected with a certain disposition (anlage). This association of tabes and a diencephalic lesion appears to be the more probable as a certain body build is to be observed frequently in tabetic persons, to which attention will be directed in the following section. This body build points to an anomaly within the hypophysiodiencephalic system, and this defect is to be considered, in addition to syphilis, as an important factor in the pathogenesis of tabes in many instances.

While studying the vegetative nervous system, Eppinger and Hess [28] noted an exaggerated response to injection of pilocarpine in some tabetic patients. Others manifested spontaneous hyperhidrosis; sialorrhea; lacrimation; painful, watery diarrhea; bradypnea, or inhibition of respiration, and hypersecretion of the vulvar and vaginal mucosa (*crises clitoridienne*). All these phenomena are in accord with the slowness with which atropine induces mydriasis, as noted in the introduction to the paper. It is of interest that the increased response to pilocarpine was observed chiefly in cases of tabes with amblyopia, demonstrating the imbalance of the vegetative sphere in this type of tabes.

### BODY BUILD OF TABETIC PATIENTS

*Juvenile Tabes Dorsalis.*—In the search for a body build characteristic of tabetic patients, the most impressive features were noticed in persons with juvenile tabes, i. e., the type with an inherited syphilitic background and developing in early adolescence (or even childhood), but most frequently at the age of puberty.

The patients, in addition to sometimes presenting signs of inherited syphilis, are thin, frail and considerably stunted in physical growth (Hough [29]). The proportions of the body in the adolescent tend to exhibit infantile characteristics. The gonads and mammary glands are underdeveloped. The menarche is delayed. Phimosis and cryptorchism may occur. In boys, the larynx is rather small and the voice high pitched.

28. Eppinger, H., and Hess, L.: Ztschr. f. klin. Med. **68**:69, 1905.
29. Hough, W. H.: J. Nerv. & Ment. Dis. **36**:577, 1909.

Secondary sexual signs are absent. Grinker [29a] noted the feminine appearance of a male patient; Brissaud and Gy,[29b] masculine features in a girl. Signs of rickets are conspicuous and frequent. At autopsy (Middlemass [24]) the uterus and ovaries were observed to be of infantile size.

It is tempting to trace both the physical and the sexual underdevelopment to one factor, a central hypophysiodiencephalic lesion. In hereditary syphilis anatomic involvement of the pituitary body is well known. In a series of 12 cases of this type of syphilis Simmonds [30] observed necrosis, gummas and inflammatory changes of the hypophysis in no less than 50 per cent. Hydrocephalus is not uncommon in syphilitic children and is apt to influence the function of the hypophysis and the vegetative center of the diencephalon.

Both infantilism and dwarfism are known to occur in children with inherited syphilis (Nonne,[31] Rolleston [31a]). This infantilism may be associated with mental retardation, amenorrhea and absence of secondary sexual characters, with signs of diencephalic disturbance (polyuria, adiposogenital dystrophy). True acromegaly, however, has never been noted in cases of congenital syphilis, which, as a destructive process, does not add to the activity of the hypophysis. In cases of tumors of the hypophysis without acromegaly, Hirsch [32] noted amenorrhea in 92.5 per cent of the women. Of these cases of tumors of the hypophysis without acromegaly he found visual disturbances in 100 per cent and primary atrophy of the optic nerve in 89 per cent. From the functional viewpoint this nonacromegalic, amenorrheic category of hypophysial growths is somewhat comparable to the hypophysial involvement occurring with congenital syphilis. According to Erdheim,[33] the genital disorders as well as the adiposity associated with diseases of the hypophysis are dependent on the destruction within the hypophysiodiencephalic system. The atrophy of the optic nerve and the destructive process within the diencephalon are, apparently, closely related.

The clinical picture of tabes juvenilis presents remarkable features. The course of the disease is mild, reminding one of Benedikt's law,[3] sometimes almost asymptomatic (except for the Argyll Robertson sign or the absence of tendon reflexes). Ataxia is of moderate degree, although Romberg's sign is present. Sphincteric disturbances of the

29a. Grinker, J.: J. Nerv. & Ment. Dis. **31**:753, 1904.

29b. Brissaud and Gy: Encéphale **1**:172, 1909; Rev. neurol. **17**:16, 1909.

30. Simmonds, M.: Dermat. Wchnschr. **58**:104, 1914.

31. Nonne, M.: Syphilis and Nervensystem, Berlin, S. Karger, 1924, p. 931.

31a. Rolleston, H.: Thesis, London, 1921.

32. Hirsch, O.: Wien. klin. Wchnschr. **39**:93, 1926; Ztschr. f. Augenh. **45**:294, 1921; Presse méd. **34**:578, 1926.

33. Erdheim, J.: Beitr. z. path. Anat. u. z. allg. Path. **46**:233, 1909.

rectum and the urinary bladder take a minor place. Lightning pains are not extremely severe. Mental development is retarded (Marburg [34]). There is no nystagmus, an important feature differentiating juvenile tabes from Friedreich's disease. The cranial nerves are not involved. So far as my limited personal experience shows, there are no signs of status dysraphicus (Bremer). Most impressive is the amazingly high incidence of primary atrophy of the optic nerve—40 per cent, according to Rosenheck. The pupils are rather large. No signs of keratitis or chorioretinitis are evident. The coincidence of primary bilateral atrophy of the optic nerve and "diencephalic" signs is noteworthy, in my opinion.

*Acquired Tabes Dorsalis.*—Endogenous Factor: The spinal cords of tabetic patients have been noted to present dystopias of the fibers and infantile proportions (Stern [13a]). Atrophy of the gonads was observed by Bitot and Sabrazès,[35] Rivière [36] and Fournier.[37] The origin of this atrophy is not clear. Should it prove to be congenital, it would be comparable to the atrophy of the testes associated with hypophysiodiencephalic disorders (Berblinger,[38] Kraus [39]).

According to the statistical studies of Mattauschek and Pilcz,[40] of 4,134 syphilitic officers of the Austrian army, dementia paralytica developed later in 4.79 per cent and tabes dorsalis in only 2.73 per cent. This remarkable observation suggests that, in addition to the precipitating infectious agent, an endogenous anomaly is requisite to the development of tabes. The rather high incidence of diabetes mellitus in the families of tabetic patients (Strohmayer [41]) is noteworthy. In families in which there appeared a certain type of tabes with adiposity, which was often associated with bilateral atrophy of the optic nerve, Stern [13b] observed adiposity and diabetes mellitus. The association of tabes or of tabetiform signs with endocrine disorders—acromegaly, as has previously been mentioned, exophthalmic goiter and Addison's disease—is interesting, since in all these conditions the presence of a lesion of the hypophysis cannot be doubted (acromegaly, with its well known anatomic background; exophthalmic goiter, in which Osler [42] suggested that the

34. Marburg, O.: Wien. klin. Wchnschr. **19**:1295, 1906.

35. Bitot, E., and Sabrazès, J.: Rev. de méd. Paris **11**:897, 1891.

36. Rivière, G.: De l'anésthesie et de l'atrophie testiculaires dans l'ataxie locomotrice progressive, Bordeaux, 1885.

37. Fournier, A.: Leçons sur la periode préataxique, Paris, 1885.

38. Berblinger, W.: Beitr. z. path. Anat. u. z. allg. Path. **89**:233, 1931.

39. Kraus, E. J.: The Hypophysis, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8, p. 810.

40. Mattauschek, E., and Pilcz, A.: Ztschr. f. Neurol. u. Psychiat. **8**:138, 1912.

41. Strohmayer, W.: Neurol. Centralbl. **26**:755, 1907; cited by Stern,[13b] p. 71.

42. Osler, W.: Principles and Practice of Medicine, edited by H. A. Christian, ed. 14, New York, D. Appleton-Century Company, Inc., 1942, p. 1168.

hypophysis played a primary role, and Addison's disease, with involvement of the adrenal gland and, besides, a distinct decrease of basophilic cells in the pituitary body, according to Crooke and Russell [43]). As for diabetes, Houssay's diabetogenic factor in the anterior lobe of the pituitary gland should be recalled. Dufour and Cottenot [44] and Thies [45] reported impairment in the condition of tabetic women during pregnancy, another indication of a possible role of the endocrine glands, particularly the hypophysis, in the course of tabes.

As for the visual disturbances associated with atrophy of the optic nerve in tabes, it was mentioned in the introduction to this paper that the visual fields for red and, particularly, for green may be contracted early in the course of tabes, whereas appreciation for blue remains intact for a longer period. This earlier loss of the fields for red and green would mean a defect of that part of Hering's *Sehsubstanz* which represents the physical substratum for red and green sensation. At present there is no means of knowing whether this defect is acquired or congenital. Establishment of its congenital origin would provide a link with color blindness (protoanopia and deuteranopia).

According to modern physiology, dark adaptation is largely dependent on the activity of the rods (Kries [46]). Consequently, the early impairment of dark adaptation in cases of tabes with atrophy of the optic nerve suggests an anomaly of the rods. Embryologically, the rods, derivatives of the outer neuroblastic layer of the bulbus, and the hypophysis make their appearance at about the same time, in the eleventh or twelfth week of embryonic life; and it is possible that a congenital structural or functional anomaly of the rods may be linked with the disturbances of the pituitary body.[47] On the other hand, it has beeen demonstrated that in this early stage of embryonic life the roof of the hypophysial pouch lies immediately on the diencephalon and so is intimately connected with the optic nerve (Hochstetter [48]).

Conclusion: I conclude that there exists a definite predisposing abnormality in patients with acquired tabes dorsalis and that there is evidence that the site of this anomaly is the hypophysiodiencephalic area.

Body Build: From Stern's [13b] extensive clinical studies, ample evidence has been accumulated that Stiller's "asthenic" body build

43. Crooke and Russell, cited by Muir, R.: Textbook of Pathology, ed. 5, Baltimore, Williams & Wilkins Company, 1941, p. 959.

44. Dufour, H., and Cottenot, M.: Bull. et mém. Soc. méd. d. hôp. de Paris **27**:211, 1909.

45. Thies, J.: Charité-Ann. **34**:591, 1910.

46. Kries, J.: Klin. Monatsbl. f. Augenh. **70**:577, 1923.

47. The function of the rods is believed to be connected with vitamin A metabolism.

48. Hochstetter, F.: Beiträge zur Entwicklungsgeschichte des Menschlichen, Vienna, F. Deuticke, 1924, vol. 2, p. 2.

(leptosomatic," according to Kretschmer[49]; "linear," according to Stockard) represents an important factor in the genesis of acquired tabes. Dementia paralytica appears to be related, rather, to the "muscular," or "lateral," type. In a series of 122 patients reported by Stern, 76 were of the "asthenic" type and 46 of the "muscular" type. Of the 76 asthenic patients, 65 had tabes, 3 dementia paralytica and 8 questionable dementia paralytica; but of the 46 patients of the "muscular" type, 22 had tabes, 14 dementia paralytica and 10 questionable dementia paralytica. This agrees with Chaillou's[50] observation that his patients with dementia paralytica had an usually well developed musculature (*type musculaire*). Signs of rickets are of frequent occurrence in tabetic patients. According to my personal experience, rickets is often to be found in asthenic patients. In a family of several children who were infected with syphilis in early childhood, Stiefler[51] noted that only the 2 asthenic members acquired tabes, the others being spared. On close examination, the asthenic body build may exhibit variations, as will be seen later. Stiefler's classic picture, however, has many features in common with that of castrated persons described by Tandler and Grosz[52]: the long, thin extremities; weak musculature; lack of muscular tone, and underdevelopment of the external sexual organs and of the secondary sexual characters. The common denominator of the two conditions may be found in a disorder of the endocrine glands, dependent in the asthenic patients on the hypophysiodiencephalic system.

Although a profound metabolic disorder and, consequently, considerable loss of weight are initial signs in a majority of cases of tabes, it is essential to make one comment:

In certain cases of tabes with rapid loss of weight (tabes marantica) one is reminded of the extreme emaciation and cachexia of Simmonds' disease, due to atrophy of the anterior lobe of the hypophysis. The syndrome of loss of weight, asthenia, amenorrhea, sterility and loss of sexual power and desire encountered in Simmonds' disease are similar to the signs and symptoms of this type of tabes dorsalis. In contrast to this type, there is a form of tabes in which the patient is comparatively well nourished and rather obese. It is in cases of this type that primary atrophy of the optic nerve is likely to develop. The course of this type of tabes is rather mild. The clinical contrast between the two categories is striking. It suggets a corresponding contrast in the makeup of the endocrine glands, notably, in the activity of the pituitary system. Certain

49. Kretschmer, E.: Körperbau und Charakter, Berlin, Julius Springer, 1936, p. 21.

50. Chaillou, A.: Clinique **6**:305, 1911.

51. Stiefler, G.: Wien. klin. Wchnschr. **22**:163, 1909.

52. Tandler, J., and Grosz, S.: Arch. f. Entwcklngsmechn. d. Organ. **27**:21, 1909; **30**:236, 1910.

structural variants of the physique may substantiate this hypothesis. In view of these indubitable facts, one is tempted to search for a relation between atrophy of the optic nerve and this category of tabes dorsalis. Does there exist a link between primary atrophy of the optic nerve and the type of physique of certain tabetic patients?

In the second and third articles in this series,[53] moreover, attention was called to the diencephalon and its vegetative center, on the one hand, and the production of glaucomatous attacks, on the other. Since in certain cases of glaucoma atrophy of the optic nerve may develop, the cause of which is unknown, does a link exist between this "glaucomatous" atrophy and the structural pattern?

The records of the following 8 cases may serve as an illustration of my point of view and as an answer to this question.[54]

CASE 1.—T. H., a man aged 72, the second of 11 children, had a history of measles, malaria, gonorrhea and syphilis thirty years before. The patient neglected his treatment for syphilis; he was given a few injections. There was no history of "crises" or of ataxia or incontinence. He complained of headache and impaired eyesight.

*Examination.*—There were dulness from the apex of the lung to the level of the first dorsal segment on the right side and sensitivity of the right brachial plexus on pressure. The breath sounds were diminished over the area of dulness. The larynx deviated to the right. The boundaries of the heart were normal; the second aortic sound was accentuated. The blood pressure was 185 systolic and 105 diastolic. Both the temporal and the radial arteries were thick and tortuous. Pulsation of the brachial arteries was visible on both sides. The malleoli, the capitulum of the ulnas, both clavicles, the parietal bones and Ludwig's angle were thick. The pupils were equal, centrally located and pinpoint in size. The Argyll Robertson sign was present; the patellar reflexes were weak, particularly on the right side. The ankle reflex was weak on both sides. Romberg's sign was not elicited. In 1929 the Wassermann test gave a positive reaction in all dilutions. After lumbar puncture the patient had a severe headache. The cell count of the spinal fluid was 87 per cubic millimeter. The colloidal gold curve was 1233210000 (1930). After tryparsamide therapy the serologic reactions of the blood and the spinal fluid were negative.

The patient was rather tall (height, 174 cm.) and lean (weight, 164 pounds [74.4 Kg.]); the circumference of the chest was 84.2 cm. The chest was long, flat and hairless; the abdomen was flat, with a circumference of 74.5 cm. There was a marked median furrow, starting close to the epigastric angle and extending down to the umbilicus. The skull was high, suggesting oxycephaly. The circumference of the skull was 56 cm. and the height 13.6. The zygomas were prominent; the chin was strong and large, with a median groove; both rami of the mandible were strong. The frontal sinuses and the glabella were prominent. The occiput was bulging. The tongue was thick and deviated slightly to the right. The teeth were large and strong. The scrotum and penis were large.

53. Hess, L.: Pathogenesis of Acute Glaucoma, Arch. Ophth. **32**:128 (Aug.) 1944; Pathogenesis of Glaucoma, ibid. **33**:392 (May) 1945.

54. The ophthalmologic data were furnished by Dr. Henry Boruchoff and Dr. Albert Elsberg, of the Beth Israel Hospital, Boston.

The feet were flat and strikingly long (the tip of the heel to the tip of the right toe was 25 cm.). The thighs and legs were thin; both hands were thin and long (length of the right index finger, 10 cm.; length of the right middle finger, 11.3 cm.).

Ophthalmic examination showed glaucomatous atrophy with characteristic cupping of the disk and opacities in the lens of the left eye. The anterior chambers of the eyes were shallow. Ocular pressure was high in each eye, with a tension of 35 to 50 mm. (Schiøtz) in the right eye and of 40 to 100 mm. in the left eye. Vision was 20/40 in the right eye and questionable in the left eye. No essential changes were apparent in the fundus of the right eye.

*Summary.*—This case was characterized by late syphilis, hypertension, a healed (tuberculous?) lesion in the apex of the right lung, mild tabes, an asthenic habitus with acromegaloid signs, unilateral atrophy of the optic nerve and glaucoma simplex.

Remarkable in this case was the fertility of the patient's mother. The patient himself had no children. I wish to stress this high degree of fertility in the family, which has not been noted in the literature. It has been noted earlier in this paper in connection with tabes juvenilis. It holds true also of juvenile dementia paralytica. Of 8 cases of the latter disease described by Nonne,[31] a high degree of fertility was evident in 6 (Nonne paid no attention to this fact). According to Nettleship,[2c] the families of patients with retinitis pigmentosa are unusually prolific. In my personal experience, this feature is not uncommon in families of feebleminded and degenerate children whom I had the opportunity to study in the Wrentham State School.

The body build of the patient is the classic "habitus asthenicus." Acromegalic traits, nevertheless, are noticeable (large chin and zygomas, pronounced frontal sinuses and glabella, strong lower jaw, large genitalia). Some of these signs may be related to rickets. The predisposition of asthenic patients to rickets has been mentioned.

Furthermore, the high skull seems to be noteworthy, reminding one of oxycephaly. In the fourth article,[16] the coincidence of oxycephaly and atrophy of the optic nerve was discussed, and the height of the skull was traced back to an abnormality of the middle fossa, with probable involvement of the diencephalon. Interestingly, in Kraus's [27] case of nanosoma pituitaria associated with congenital hypoplasia of the optic nerves the skull was surprisingly high (index, [height/length] 76.6) and pointed. In nanosoma pituitaria without atrophy of the optic nerve the skull is short, brachycephalic or hyperbrachycephalic, but not high. This fact should be borne in mind.

I have noticed the long hands and feet (cheiromegaly and podomegaly) in a great many children with disproportionate growth.

The tabes in this case was mild, almost asymptomatic.

The diagnosis of "glaucoma simplex" was established on the basis of the principal signs; there were no signs of acute congestion. The

unilateral atrophy of the optic nerve was undoubted. Its relation to tabes cannot be ruled out, as the atrophy of the fellow nerve may occasionally develop several months or years later.

Case 2.—G. S., a housewife, aged 52, the second of 8 children, had had measles and whooping cough during childhood. In 1917 she had a "genital sore," which was "irregularly" treated with injections. The menarche occurred at the age of 11; the menses were regular and painful. The menopause occurred at the age of 46, without difficulty. She was delivered of 1 child, who died at the age of 6 weeks.

*Examination.*—Examination revealed dulness of the apex of both lungs, with dilated superficial Kuty veins in this area and diminished breath sounds. There were dilated subcutaneous veins on the anterior aspect of the chest and cor pendulum. The heart tones were of good quality; the blood pressure was 145 systolic and 70 diastolic. Both pupils were small; the left one was spherical and the right one irregular in shape; both were fixed to light but reacted to distance. The abdominal reflexes were normal on the left side; those on the right were absent (postoperative scar). The knee and ankle reflexes were normal; the Romberg sign was not elicited. There was a zone of hypalgesia below the right breast. Lumbar puncture, performed with the patient in the reclining position, revealed an initial pressure of 80 mm.; after removal of 10 cc. of fluid the pressure was 25 mm. The total proteins measured 50 mg. per hundred cubic centimeters. The reaction for globulin was negative. The Wassermann-Hinton reaction of the fluid was negative. The cell count revealed 1 cell per cubic millimeter. The patient was black haired, tall (height, 170 cm.), slender (weight, 98 pounds [44.5 Kg.], never exceeding 128 pounds [58.1 Kg.]) and leptosomatic (chest flat, axillary and genital hair and eyebrows scanty), with prominent acromegaloid signs (large, plump fingers and toes; heavy, high chin; large mandibular rami; large upper incisors, widely separated; large tongue, with a median and a pronounced lateral fissure), and high forehead.

The left eye showed deep glaucomatous cupping of the optic nerve head and atrophy of the nerve. There was complete absence of vessels temporally. Both anterior chambers were shallow. The patient experienced no pain in the eye.

Tension was 35 mm. (Schiøtz) in the right eye and 90 mm. in the left eye. Vision was 20/20 in the right eye and doubtful in the left eye.

*Summary.*—There were fibrotic changes in the apexes of both lungs, mild tabes, an asthenic habitus with acromegaloid features, glaucoma simplex and unilateral atrophy of the optic nerve.

Remarkable in this case are the fertility of the patient's mother (the patient herself had only 1 child) and the mild course of the tabes. The glaucoma was almost painless, as are many conditions (childbirth, pneumonia) in cases of tabes.

Case 3.—A. K., a Russian Jew aged 56, was the fifth of 11 children. His father, one of 17 children, died at the age of 83, of old age. His mother died at the age of 84, of heart disease. There was a past history of tonsillectomy, chronic suppurative otitis media with perilabyrinthitis and syphilis (1918), which was treated with arsphenamine, tryparsamide and a preparation of mercury. The patient did not drink or smoke. He complained of dizziness, headache, sleeplessness and blurred vision.

*Examination.*—There were slight cyanosis of the lips. Dulness was noted on the right side from the apex of the lung down to the second dorsal segment, with slight atrophy of the right trapezius and supraspinatus muscles and bronchial breathing over that area. The trachea and larynx were displaced to the right side. The boundaries of the heart were found on percussion to be the right sternal border, the third rib and the left midclavicular line. Fluoroscopic examination revealed a distance from the midline of 4.8 cm. to the right border and of 9.8 cm. to the left border and a transverse diameter of 14.6 cm. (enlargement of the left ventricle). A soft systolic murmur was heard over the entire precordium. The second aortic sound was not accentuated. An electrocardiogram showed left axis deviation and a prolonged P-R interval (myocardial damage). The edge of the liver was about 2 fingerbreadths below the costal margin. The spleen was not enlarged. The blood pressure was variable, at times being 190 systolic and 120 diastolic and at others 220 systolic and 120 diastolic. Nodal piles were present. The pupils were equal and narrow, with a bilateral Argyll Robertson sign. The patellar reflex was diminished on both sides. The achilles reflex was more active on the right side than on the left. All abdominal reflexes were missing except in the left upper quadrant. The Romberg sign was not elicited. The Wassermann reaction of the spinal fluid was positive in 1919 and later became negative.

The patient was of medium size (height, 167 cm.) and obese (weight, 162 pounds [73.5 Kg.]). The cheeks and nose were reddish; the nose was snub, and the forehead was large but not high. The neck was short and thick. The shoulders were rounded, with a pronounced deltoid-pectoral furrow. The chest was large and deep—almost barrel shaped. The hands were soft, short and broad. The legs were rather thin. The pelvis was large and of feminine type. There were deposits of fat on the lower part of the abdominal wall and on the thighs. A deep furrow was present above each knee. Gynecomastia was present. Both testes were small and soft; he had had no erection for ten years. The pubic hair was of horizontal outline, but a few hairs were present along the linea alba. The back and chest were hairless except for a few short hairs toward the lower part of the sternum. There were few hairs on the anterior aspect of the lower part of the legs. The eyebrows were scanty, particularly laterally. The skull was large, with a circumference of 57.3 cm. and a sagittal diameter of 18.9 cm. The bifrontal diameter was 15.8 cm.; the cephalic index, 84.6. The palate was large and the chin heavy.

Tension was 43 to 45 mm. (Schiøtz) in the right eye and 55 to 75 mm. in the left eye; vision was 10/20 in the right eye and consisted of light perception with projection temporally and below in the left eye. There was bilateral atrophy of the optic nerve with glaucomatous cupping. Degenerative patches were present in the retina of the left eye. Both anterior chambers were shallow.

*Summary.*—The case was characterized by late syphilis, slowly progressive nephrosclerosis with myocardial damage, fibrotic changes in the apex of the right lung, hemorrhoids, chronic otitis media, mild tabes, pyknic habitus with genital disturbance, bilateral atrophy of the optic nerve and glaucoma (diagnosed many years ago).

Noteworthy are the longevity of the patient's family, the mild course of the tabes, the classic pyknic habitus combined with genital disorders (soft testes, impotency, gynecomastia, female type of pelvis, feminine distribution of pubic hair, scanty hair on the body) and acromegaloid signs (strong chin, large tongue, scanty eyebrows).

It seemed of interest to describe briefly these 3 cases representing the association of glaucoma simplex with mild tabes. The glaucoma was practically painless. In 2 cases the asthenic type of body build was combined with acromegaloid signs; in the third case the pyknic habitus, which is rare in tabetic patients, was combined with genital disorders.

Three cases of glaucoma not complicated with tabes may be summarized from the standpoint of constitutional type.

CASE 4.—N. S., a Negro aged 52, had a history of gonorrhea in 1908 and of syphilis in 1918. The syphilis had been treated with a bismuth compound. His wife had had 3 or 4 miscarriages. The patient had always been strong and able to lift heavy weights. The muscles of his arms and legs were unusually strong and of athletic volume. The testes and the scrotum, however, were small, the skin of the latter being soft, thin and unwrinkled. The pubic hair was horizontal in outline and scanty. The chest, abdominal wall, axillas and both arms were hairless, but a few hairs were noted near the lateral aspect of the upper and lower portions of the legs. The chin was heavy and large. The zygomas and the glabella were large.

There were no clinical signs of neurosyphilis. The Wassermann-Hinton and Kahn reactions of the blood were negative.

Tension was 32 mm. (Schiøtz) in the right eye and 27 mm. in the left eye. Vision was 20/50 in the right eye and 20/30 in the left eye. The optic disk of the right eye was atrophic and pale, with a deep excavation near the margin of the disk. A surgical coloboma marked the site of an operation performed several years ago because of an acute attack of pain. The disk of the left eye was normal.

*Summary.*—The case was one of late syphilis and glaucoma with unilateral atrophy of the optic nerve.

Kretschmer[49] expressed the belief that the combination of "dysgenitalism" and the athletic body build is not uncommon. It certainly indicates an abnormal development due to a diencephalic factor. Cases of glaucoma have been recorded in the literature in which antisyphilitic treatment was to some extent successful. I venture to surmise that these old cases may have been instances of arrested or mild neurosyphilis associated with glaucoma.

CASE 5.—L. M., a housewife aged 67, had had the menarche at 17 ("was given medicine for it") and the menopause at 47. The menstrual periods were always irregular and painful. She had had 3 miscarriages and 4 deliveries.

The patient was of the adipose-pyknic type, with deposits of fat on the thighs and the abdominal wall, the arms and chest being spared. The mammary glands were poorly developed (she had been unable to nurse any of her children). Her weight was 177 pounds (80.3 Kg.), and her height, 169 cm.; her face was "pentagonal." There were no signs of old rickets.

Tension was 32 mm. (Schiøtz) in the right eye and 40 mm. in the left eye. Vision was 20/30 in the right eye and 20/30 in the left eye.

No nasal contraction of the visual fields was noted. There were pronounced cupping and atrophy of both nerve heads.

*Summary.*—The patient was of adipose-pyknic type with "dysgenitalism." She presented glaucoma with bilateral atrophy of the optic nerve and moderately increased

ocular pressure at the time of the examination. (The patient showed a certain tendency to "fertility").

CASE 6.—S. C., a man aged 70, was a Russian Jew, the youngest of 6 siblings. His father died at the age of 75; he had had trouble with his feet (senile gangrene?); his mother died at about the same age, of an unknown disease. The patient was married and had 7 children; 1 child was born blind and "without a brain"; 1 son was stated to be an inmate of a state hospital for a disease believed to be incurable (dementia precox?). The patient could not control his bladder until the age of 6 (nocturnal enuresis?). He had typhoid at 16 and an attack of "rheumatic fever" at 20, with no recurrence. In recent weeks he had experienced a sensation of pressure on the chest after excitement or on climbing stairs. The pain was controlled by glyceryl trinitrate. The patient had been a heavy smoker for years. There was no history of alcoholic abuse or of venereal disease. He had always been stout and fat, his weight ranging from 200 to 205 pounds (90.7 to 93 Kg.); he had lost about 5 pounds (2.3 Kg.) in recent weeks. Bowel movements and appetite were normal.

*Physical Examination.*—When the patient was first seen, his weight was 198 pounds (89.8 Kg.), and his height, 5 feet 7½ inches (171.5 cm.). There was no cyanosis or peripheral edema; the veins of the neck were not distended. Both radial arteries were thin; the pulse was slightly irregular; the blood pressure was 140 systolic and 70 diastolic. The boundaries of the heart were the third rib, the right sternal border and the left midclavicular line. The heart beat was not palpable; the sounds were of good quality but distant. There was immobility of the base of the left lung with small dilated veins over this area (Sahli's wreath). The urine was normal; the Wassermann-Hinton reaction of the blood was negative; the electrocardiogram showed premature auricular beats, a rate of 65 per minute, left axis deviation, an inverted T wave in lead III and a normal lead IV.

The patient was stout and rather obese, with deposits of fat on the lower part of the abdominal wall and a deep transverse fold above the symphysis. Fat was abundant on both thighs, with less on the upper parts of the arms. The chin was double; the neck was short and large. The nasolabial folds were deep. The nose was rather thick; the nostrils were wide; the tip of the nose and the cheeks were reddened. The skull was large and of mesaticephalic type. The measurements were as follows: bitemporal diameter, 14.0 cm.; bimaxillary diameter, 10.0 cm.; sagittal diameter, 18.5 cm.; height, 21.5 cm. The cephalic index was 75.6. The circumference was 57.3 cm. The vertex was flat and the occiput moderately bulging. The face was broad; the mandibles were slightly curved, with a moderate amount of fat on the lateral portions. The lateral contour of the face was almost vertical. The palate was large. The pubic hair was horizontal, with only a few hairs along the linea alba. A group of dark hairs was confined to the sacral area. The axillas and the four extremities were hairless. (The beard had never been strong.) The testes were small and soft (due to age?). The prostate was not enlarged. There were no definite signs of rickets. The chest was large and short, suggesting the "barrel chest," with wide, symmetric costal angles. The tip of the spleen was palpable. The liver was not enlarged. The deep, cutaneous and right pupillary reflexes were normal.

*Ophthalmic Examination.*[55]—In January 1940 the patient stated that for about a year he had had attacks of blurring at night, which cleared up in the morning. Two

55. The ophthalmologic data were furnished by Dr. Benjamin Sachs, of the Beth Israel Hospital, Boston.

weeks prior to examination he had considerable pain and blurring in the left eye. Examination revealed severe congestive glaucoma in the left eye, with considerable steaminess of the cornea and practically no anterior chamber. The pupil of this eye was widely dilated. Tension was 66 mm. (Schiøtz). Vision consisted only of light perception. The right eye had normal tension but a very shallow anterior chamber. Mecholyl and neostigmine were administered to the left eye, with little influence on the pressure. A paracentesis was performed. The miotics had no effect on the tension. An iridectomy was done. Tension was controlled, and vision improved. By May the tension was within normal limits. Both anterior chambers were very shallow. The left iris was atrophic. The right optic disk was normal. The left optic nerve was atrophic. Vision was 20/40 in the right eye with glass (high hyperopia with hyperopic astigmatism) and 20/50 in the left eye.

*Summary.*—The patient was of pyknic type with "dysgenitalism," unilateral "glaucomatous" atrophy of the optic nerve, healed pleurisy of the left side and hypertrophy of the left ventricle.

The following 2 cases of mild tabes may serve to illustrate both the pyknic-dysgenital and the asthenic-acromegaloid category of the disease. Neither patient had glaucoma.

CASE 7.—S. I., a Portuguese aged 40, complained chiefly of blurred vision in both eyes, of about nine months' duration. There was no history of syphilis. The Wassermann-Hinton tests of the blood and the spinal fluid, however, gave positive reactions.

Both pupils were miotic and fixed to light, with a normal reaction in accommodation. Both the ankle and the knee jerks were absent. The Romberg sign was not elicited. The cremasteric and abdominal reflexes were hyperactive. There was no mental deterioration.

The patient was well nourished (with no notable loss of weight in recent months). The skull was rather high and of hypsicephalic type (bregma-chin measurement, 13.8 cm.). There were a double chin and deposits of fat on the abdominal wall, the thighs and buttocks. The chin was short and large, with two pads of fat. The bridge of the nose was sunken. The glabella was rather large and prominent. The legs and fingers were thin and delicate, the latter being long and hyperextensible. The thorax was short and large and covered with hair. The testes were small and soft and were not sensitive to pressure. The pelvis was large, of feminine type. No sign of rickets was apparent. Atrophy of the optic nerve was present bilaterally, with both fields contracted peripherally. The ocular pressure was normal. Vision was 20/30 in each eye.

*Summary.*—The patient had tabes dorsalis, oligosymptomatic (with no history of "crises" and no pronounced ataxia), and bilateral primary atrophy of the optic nerve. He was of pyknic habitus with a tendency to female adiposity and a certain degree of dysgenitalism. He had no history of initial loss of weight.

CASE 8.—A man aged 74, a painter, had been troubled for four or five years with sharp pains in the left leg, of sudden onset and short duration. The eyesight had begun to fail. The bowels were regular. The bladder was continent. Bilateral herniorrhaphy had been performed five years before. He had 5 children, all of whom were reported to give negative serologic reactions of the blood.

The pupils were unequal and of irregular size, reacting sluggishly to light and better in accommodation. The mobility of the eyeballs was not restricted. There

was no nystagmus. The knee and ankle reflexes were absent. The Romberg sign was not elicited. The patient walked with a broad base. There were no prominent sensory defects. The Hinton reactions of the blood and spinal fluid were negative. The reaction of the fluid for globulin was positive. The cell count was 198 per cubic millimeter. The colloidal gold curve was 5544321100. The total protein was 62 mg. per hundred cubic centimeters. Both disks were pale; they presented no inflammatory changes. Both fields were contracted peripherally. Ocular pressure and the anterior chambers were normal.

The patient was tall (height, 5 feet 6 inches [167.5 cm.]), lean (weight, 147 pounds [66.7 Kg.]) and pale. He was euphoric. The skull was of hypsicephalic type. The chest was long and flat, with an acute epigastric angle. The tenth rib fluctuated on each side. Moderate deposits of fat were present on the upper portions of both arms (of feminine distribution) and on the abdominal wall. The trunk and all the extremities were hairless. The chin was large and high, with two grooves. The fingers and toes were large and plump. The nose was large. The pubic hair was scanty.

*Summary.*—The patient presented tabes dorsalis, oligosymptomatic; bilateral atrophy of the optic nerve; acromegaloid signs, and a tendency to the feminine type of obesity. There were undoubtedly signs of asthenic habitus: The flat, long chest with the acute epigastric angle, the fluctuating ribs, the tendency to herniation (frequent, in my personal experience, with the asthenic habitus) and the scanty pubic hair (which had always been so) were evidence. But at first glance the picture of "asthenia" might be obscured by the acromegaloid signs (large chin, large toes and fingers, large nose) and the tendency to adiposity. These transitional forms are theoretically important, as they are indicative of a participation of the hypophysiodiencephalic system.

## COMMENT

The rare occurrence of tabes in syphilitic patients (in about 2 per cent) compares well with the infrequency of nervous complications following certain other infectious diseases (diphtheria, influenza, malaria) or toxic conditions (alcoholism). It demonstrates that an endogenous factor is decisive in the pathogenesis of certain anatomic diseases of the central nervous system.

As for the endogenous agent operative in acquired tabes dorsalis, Stiller's habitus asthenicus deserves attention, because in a majority of tabetic persons objective clinical signs or subjective symptoms (weakness, fatigue, vague pains) of this type of organization can be observed. There are indications that in the asthenic type the hypophysiodiencephalic system is involved, at least so far as sexual disturbances, physical underdevelopment and a tendency to association with hypophysial disorders are concerned. In certain cases of tabes unquestionable signs of diencephalic origin can be detected. Of the cases of acquired tabes there is a small number, about 15 per cent, associated with primary atrophy of the optic nerve, whereas in cases of juvenile (congenital) tabes this proportion is much higher (40 per cent, or even 60 per cent according to some authors).

It is known that in cases of congenital syphilis the pituitary body frequently shows anatomic alteration. This change, together with the stunted growth and sexual retardation, may be considered evidence of a congenital anomaly of the hypophysiodiencephalic area. It leads one to compare the rather frequent occurrence of atrophy of the optic nerve in cases of juvenile syphilis with the frequent occurrence of optic atrophy with certain nonacromegalic tumors of the pituitary body. There might be a link between primary atrophy of the optic nerve and dyspituitarism in cases of juvenile tabes.

The mild course of juvenile tabes is similar to the well known mild course in the cases of acquired tabes with associated bilateral atrophy of the optic nerve. The mild, amaurotic form of acquired tabes presents either the asthenic habitus combined with acromegaloid features [56] or the pyknic habitus combined with signs of adiposogenital dystrophy.[57] The body build is the *conditio sine qua non* for the development of atrophy of the optic nerve.

Both the acromegaloid signs and the signs of adiposogenital disturbance being correlated with a change in the diencephalon, the atrophy of the optic nerve associated with acquired tabes may have the same pathogenesis as the atrophy occurring with juvenile tabes.

The diencephalic lesion under discussion is essentially a minute congenital anomaly of the brain. On the basis of this anomaly, the atrophy of the optic nerve is later precipitated by syphilis. This congenital lesion may provide a clue to the understanding of some clinical peculiarities of atrophy associated with tabes (early impairment of dark adaptation, a possible link with color blindness, or daltonism).

Atrophy of the optic nerve associated with tabes is not analogous to degeneration of the posterior roots, as has been assumed by many authors. With pernicious anemia at least, in which degeneration of the posterior roots and spinal column is frequent (in about 60 per cent of cases according to Hurst), atrophy of the optic nerve is rare. Apparently, in pernicious anemia the important hypophysiodiencephalic factor is missing.

Tabetic atrophy of the optic nerve is combined neither with nystagmus nor with cataract. As was pointed out, there are no signs of mechanical pressure on the optic nerves, nor are there any signs of inflammation.

Tabetic atrophy of the optic nerve is to be considered a systemic degeneration within the central optic pathways, between the bulbus and the primary optic centers of the brain. From the clinical standpoint, it may be compared to a certain category of primary atrophies of the optic

56. Uhthoff.[1] Oliver.[2] Deutsch.[8]

57. Benedikt.[3] Stargardt.[7]

nerve characterized by coincidence of the atrophy with diencephalic signs and a congenital anomaly within the middle fossa (Hess [16]).

As regards the nature of this lesion, the possibility of a trophic disturbance should be borne in mind. In the light of modern research (Warkany [58] and his co-workers) there appears to exist a connection between congenital malformations and nutritional disturbances.

The coincidence of "mild" tabes and glaucoma is not without interest. In some sense, it may corroborate the hypothesis that the main clinical signs of glaucoma are dependent on involvement of the diencephalon (Hess). The body build of patients with glaucoma and atrophy of the optic nerve is the same as the body build of patients with tabes complicated with amaurosis.

The body build, if early recognized and evaluated, would provide an indication to the further course of the disease. How far the management of the condition may be influenced by this concept will be discussed in the next paper. Although the significance of mechanical pressure in the pathogenesis of "glaucomatous" atrophy of the optic nerve cannot be neglected, the diencephalic factor deserves further study.

Like the primary atrophy of the optic nerve encountered with certain diseases of the middle fossa (oxycephaly, hypertelorism, certain tumors of the pituitary gland, Friedreich's disease, arachnoiditis interchiasmatica, retinitis pigmentosa, arachnodactyly and infantile myxedema) and with pregnancy, and like the atrophy of the optic nerve in certain cases of tabes dorsalis, "glaucomatous" atrophy of the optic nerve may be connected with a congenital anomaly of the diencephalic area. The site of the glaucomatous attack and that of the congenital anomaly would be located in the close neighborhood of the vegetative center of the diencephalon. It is well to remind oneself that the optic nerve is connected with many parts of the diencephalon (nucleus supraopticus and tuber cinereum) by anatomically well defined tracts (tractus retinosupraopticus and the medial and lateral tractus retinotuberales) serving the transmission of impulses directly from the retina to the pituitary system.

## GENERAL CONCLUSIONS

Two features are prominent in glaucoma: increased intraocular pressure and atrophy of the optic nerve. The pain, although important, remains in some cases more or less in the background.

The intraocular pressure depends mainly on a neural regulation initiated by means of reflexes. The receptor organ of this reflex action is the ciliary ganglion. This is the only sensory center for all stimuli arising within the bulbus.

---

58. Warkany, J.: Congenital Malformations Induced in Rats by Maternal Nutritional Deficiency, Am. J. Dis. Child. **65**:882 (June) 1943.

Glaucoma is essentially a neuroregulatory disturbance. It either starts suddenly, like a "crisis," or develops insidiously. Glaucoma is always "secondary."

The eyeball is a viscus and is "represented," as are all visceral organs, in the diencephalon. This "vegetative" center is subject to influences from the cortex (anxiety, nervous strain). In any case of glaucoma the primary site is thought to be in one of the following structures: (1) the peripheral nerve terminals within the bulbus, (2) the ciliary ganglion, (3) the diencephalon or (4) the cortex.

The therapy, if rational and, in compliance with the requirements in different cases, is to be directed to the terminal nerves, to the diencephalon or to the cortex. (The terminal nerves and the ciliary organ represent one unit.) Miotics act on the terminal nerves.

Atrophy of the optic nerve complicating glaucoma is associated with increased intraocular pressure. Aside from the pressure mechanism, there exists in certain cases of glaucoma a definite tendency to atrophy of the optic nerve. This tendency depends on a congenital anomaly, and the pressure mechanism in these cases acts as a precipitating factor.

This "glaucomatous" atrophy of the optic nerve bears a similarity to the atrophy associated with certain organic diseases of the brain. The latter type of atrophy is based on a structural anomaly of the skull (middle fossa) and of the brain (diencephalon).

Atrophy of the optic nerve is prone to develop either in persons with asthenia associated with acromegaloid features or in those with a pyknic body build associated with signs of adiposogenital disturbance. Early study of many cases from the neurologic-constitutional standpoint will assist in making the prognosis and possibly in preventing atrophy of the optic nerve.

16 Kenwood Street, Brookline 46, Mass.

# GONORRHEAL IRITIS

## Experimental Production in the Rabbit

MAURICE J. DRELL, M.D.
SEATTLE
AND
C. PHILLIP MILLER, M.D.
AND
MARJORIE BOHNHOFF, S.B.
CHICAGO

### GONORRHEAL IRITIS IN MAN

THE RECOGNITION of gonorrheal iritis has been delayed by several factors. First, Hunter's classic self inoculation resulted in gonorrhea and syphilis being considered for decades as manifestations of a single disease. Second, the association of iritis with arthritis of various kinds, including the gonorrheal, served to complicate matters. Third, gonorrheal iritis tended to be mistaken for the more commonly encountered purulent gonorrheal conjunctivitis, from which it had to be distinguished.

The clinical picture of gonorrheal iritis slowly emerged from the case reports and studies of Brodie,[1] Vetch,[2] Travers,[3] Frick,[4] Lawrence,[5] Mackenzie,[6] de Wecker,[7] Förster,[8] Fournier and Galezowski,[9] Hutchin-

From the Department of Surgery (Division of Ophthalmology); the Department of Medicine, and the A. B. Kuppenheimer Foundation of the University of Chicago.

The major portion of the work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago.

1. Brodie, B. C.: Pathological and Surgical Observations on Diseases of the Joints, London, Longman, Hurst, Rees, Orme and Brown, 1818, pp. 55-59.

2. Vetch, J.: A Practical Treatise on the Diseases of the Eye, London, G. Whittaker and W. B. Whittaker, 1820, pp. 243-246.

3. Travers, B.: A Synopsis of the Diseases of the Eye, ed. 2, London, Longman, Hurst, Rees, Orme and Brown, 1821, p. 129.

4. Frick, G.: A Treatise on the Diseases of the Eye, Baltimore, Fielding Lucas Jr., 1823, p. 42.

5. Lawrence, W.: A Treatise on the Diseases of the Eye, London, John Churchill, 1833, pp. 233-237; Washington, D. C., Duff Green, 1834, pp. 186-189; ed. 4, edited by I. Hayes, Philadelphia, Blanchard & Lea, 1854, pp. 309-312 and 347.

6. Mackenzie, W.: A Practical Treatise on the Diseases of the Eye, London, Longman, Rees, Orme, Brown and Green, 1830, pp. 376-381; Boston, Carter, Hendee & Company, 1833, pp. 312-316; ed. 4, Philadelphia, Blanchard & Lea, 1855, pp. 534-537.

*(Footnotes continued on next page)*

son,[10] Griffith,[11] Lawford and others,[12] Beaumont,[13] Cobbledick [14] and many others.

Proof of the gonorrheal origin of the iritis was slow in forthcoming. Of necessity, it had to wait on the discovery by Neisser [15] in 1879 of the gonococcus and its subsequent growth in culture by Bumm.[16]

In 1897 Karsnitski [17] published the detailed report of a case of gonorrheal iritis appearing a month after the onset of acute gonorrheal urethritis and a week after its subsidence. Examination of pus obtained by paracentesis from the anterior chamber revealed intracellular gonococci "identical with those of the previously examined urethral pus." In 1911 Sidler-Huguenin [18] reported the results of blood cultures and cultures of material from the anterior chamber of 5 patients with gonorrheal iridocyclitis. The blood cultures of 3 of the patients were positive, and material obtained from the anterior chamber of 1 of them yielded a pure culture of gonococci. The author concluded that the ocular complication was hematogenous. All 5 patients also showed optic neuritis.

Byers, in 1907, published a comprehensive monograph,[19] which is probably the best work on the ocular metastasis of gonorrhea. In it

7. de Wecker, L., in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1874, vol. 4, pt. 1, pp. 497-498.

8. Förster, in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1877, vol. 7, pt. 5, pp. 86-87.

9. Fournier and Galezowski, cited by Byers.[19]

10. Hutchinson, J.: A Report on the Forms of Eye-Disease Which Occur in Connexion with Rheumatism and Gout, Ophth. Hosp. Rep. **7**:287-332 and 455-493, 1873; **8**:191-216, 1876.

11. Griffith, J.: Iritis, a Sequel of Gonorrhoea, Tr. Ophth. Soc. U. Kingdom **20**:83-92, 1900.

12. Lawford, J. B.; Hamilton, R. J.; Yeld, R. A.; Darier, A.; Power, H.; Cross, F. R.; Drake-Brockman, E. F.; Stephenson, S.; Marshall, C. D.; Cargill, L. V., and Roll, G. W., in Discussion on the Relation of Gonorrhoea to Disease of the Eye (Excluding Purulent Ophthalmia), Brit. M. J. **2**:1330-1332, 1901.

13. Beaumont, W. M.: Remarks on Iritis, with Special Reference to Gonorrhoeal Iritis, Brit. M. J. **2**:138-140, 1908.

14. Cobbledick, A. S.: Gonorrhoeal Iridocyclitis with Observations on Its Relation to So-Called Rheumatic Iritis, Ophthalmoscope **10**:703-707, 1912.

15. Neisser, A.: Ueber eine der Gonorrhoe eigentümliche Micrococcusform, Centralbl. f. d. med. Wissensch. **17**:497-500, 1879.

16. Bumm, E.: Menschliches Blutserum als Nährboden für pathogene Mikroorganismen, Deutsche med. Wchnschr. **11**:910-911, 1885.

17. Karsnitski, A. V.: A Case of Gonorrheal Iritis, Voyenno M. J. (med.-spec. pt.) **190**:824-829, 1897.

18. Sidler-Huguenin: Ueber metastatische Augenentzündungen namentlich bei Gonorrhöe, Arch. f. Augenh. **69**:346-378, 1911.

19. Byers, W. G. M.: A Study of the Ocular Manifestations of Systemic Gonorrhoea with Reports of Cases of This Nature, Stud. Roy. Victoria Hosp. **2**: 107-231, 1908. Dr. Byers furnished us with a copy of his monograph and granted us permission to reproduce an illustration (fig. 1, p. 163) from it.

he reported the first histologic study of a case of gonorrheal iritis. Since this monograph is not easily available, the illustration is reproduced (fig. 1). The patient was a young man with gonorrhea, polyarthritis and septic fever. Six weeks after the onset of the disease his left eye was the site of mild but well defined iritis. The eye was recovering satisfactorily under treatment when obscure gastrointestinal symptoms set in and the patient died; the cause of death was acute dilatation of the stomach. Histologic examination of the eyeball showed keratic precipitates on the posterior surface of the cornea, swelling and small round cell infiltration of the iris, swelling and dense cellular invasion of the ciliary body and a rather massive fibrinocellular exudate along the whole

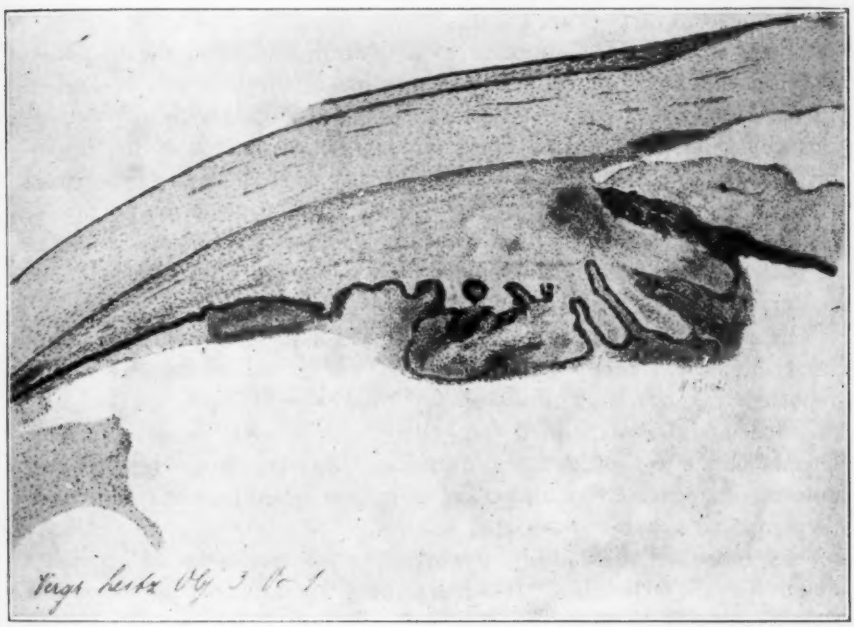


Fig. 1.—Microscopic section from Byers;[19] case of gonorrheal iridocyclitis.

extent of the ciliary processes. A differential count of the cells in the exudate showed that small mononuclear cells predominated over polymorphonuclear forms. Careful search with various stains for gonococci and other possible organisms gave negative results. Particularly striking were the degree and extent of anatomic involvement, in contrast with the mild gross clinical findings.

Roosa,[20] in 1906, reported a case of "gonorrheal metastatic iridocyclitis," although the evidence for its gonorrheal origin was inadequate.

20. Roosa, D. B. St. J.: A Case of Metastatic Gonorrheal Choroiditis: Enucleation of the Eye, Post Graduate **21**:692-693, 1906.

Similarly, in Kravitz'[21] case of gonorrheal endophthalmitis following cataract extraction the diagnosis was made merely on the presence of intracellular and extracellular diplococci, identified by the pathologist as gonococci, in the conjunctival smear.

Velhagen,[22] in 1937, published the report of a case of iridocyclitis in which histologic study of the enucleated bulb revealed organisms which he considered to be gonococci. The tenability of this conclusion is open to question, since it was based solely on the intraocular presence of gram-negative diplococci, and no gonococci or other evidence of gonorrhea was ever observed elsewhere in the patient. Velhagen did not consider the meningococcus as a possible etiologic agent. It is an organism almost identical morphologically with the gonococcus, and meningococcus carriers are not uncommon in healthy population groups.[23] Granted Velhagen's assumption of a gonococcic origin, the histologic observations were interesting. The capsule of the lens was broken on its anterior aspect, and the anterior chamber was filled with innumerable pus cells and swollen lens fibers, among which clumps of the microorganisms were visible. The iris was greatly edematous and hyperemic; the ciliary body was infiltrated with pus, and the posterior portion of the lens was embedded in a purulent mass containing numerous colonies of bacteria. The iris and the ciliary body contained no organisms. The posterior segment was only slightly involved.

In addition to the cases of optic neuritis associated with gonorrheal iritis cited by Byers[19] and Sidler-Huguenin,[18] additional cases were reported by Krause,[24] Cobbledick[25] and von Hippel.[26] The last-mentioned author expressed the belief that the optic neuritis was the chemotactic effect of a toxin diffusing backward from the inflamed anterior segment. Byers also collected 6 cases of optic neuritis in which there was no apparent associated iritis.

As encountered clinically, gonorrheal iritis manifests no especially diagnostic characteristics. It occurs much more commonly in males than in females. It generally does not arise until a few weeks after the initial genitourinary infection, and then often in association with other

21. Kravitz, D.: Postoperative Endogenous Infections of the Eye, Am. J. Ophth. **19**:328-330, 1936.

22. Velhagen, C.: Eitrige Iridocyclitis mit Gonokokken in Augeninnern, Klin. Monatsbl. f. Augenh. **98**:20-23, 1937.

23. Miller, C. P.; Beadenkopf, W. G.; Peck, D., and Robbins, M. W.: A Survey of Chronic Meningococcus Carriers in a Semi-Permanent Population, J. Infect. Dis. **74**:212-224, 1944.

24. Krause, P.: Zwei Fälle von Gonokokkensepsis mit Nachweis der Gonokokken im Blute bei Lebzeiten der Patienten, Berl. klin. Wchnschr. **41**:492-494, 1904.

25. Cobbledick, A. S.: Gonorrhoeal Iritis Complicated by Interstitial Optic Neuritis, Ophthalmoscope **10**:319-320, 1912.

26. von Hippel, E.: Ueber einen Fall von ungewöhnlich schwerer gonorrhoischer Iridocyclitis und Neuritis optica, Arch. f. Ophth. **94**:355-360, 1917.

evidences of systemic spread (arthritis, septicemia, endocarditis, or subcutaneous abscesses). Some urologists have noted so close a correlation between the onset of the iritis and instrumentation or massage that 1 of them [27] has even recommended chemotherapy during these procedures.[28] Indeed, the drastic manipulative therapy of gonorrhea in males, in contrast with the more conservative treatment of the disease in females, may account for the greater incidence of iritis (and other metastatic complications) in the male.

The classic ocular picture is that of severe anterior uveitis, with grayish, gelatinous exudate virtually filling the anterior chamber, sometimes with hypopyon and at other times with hyphema. After a few weeks the process subsides and recovery is complete, often without a single synechia. Another type of gonorrheal iritis is said to be characterized by the formation of extensive posterior synechias, multiple recurrences and eventual atrophy. Also attributed to gonorrhea is a simple, mild iritis in which complete recovery generally occurs whether or not treatment of any sort is instituted. How large a proportion of the cases of "one day iritis" fall into this category is a matter for speculation, since a thorough investigation is not usually made and the subject does not appear to have been of sufficient importance to have warranted much study.

Among reports in the literature of this century, Collins and Silcock [29] stated that gonorrhea was the causative factor in 15 per cent of 100 cases of iritis; Yeld,[12] in 8 per cent of 159 cases; Chevallereau and Chaillous,[30] in 7 per cent of 131 cases; Gutmann,[31] in 3 per cent of 150 cases; Straub,[32] in 3 per cent of 161 cases; Goulden,[33] in 11 per cent of 179 cases; Irons and Brown,[34] in 5 per cent of 200 cases; Bulson,[35] in

27. Herrold, R. D.: Chemotherapy of Gonococcic Infections, St. Louis, C. V. Mosby Company, 1943, p. 76.

28. Among others, Ward (Brit. M. J. **1**:755-758, 1901), Hamilton,[12] Browning (Brit. J. Ophth. **4**:102-106, 1920) and Holloway (Am. J. Ophth. **14**:232-238, 1931) have pointed out the association of traumatic therapy and the origin or exacerbation of systemic gonorrheal processes.

29. Collins, and Silcock, in discussion on Griffith.[11]

30. Chevallereau, A., and Chaillous, J.: Recherches sur l'etiologie de l'iritis, Compt. rend. Cong. internat. (Lucerne), 1904, pp. 310-313.

31. Gutmann, A.: Beitrag zur Aetiologie und Statistik der primären Iritis, Deutsche med. Wchnsch. **31**:1671-1673, 1905.

32. Straub, M.: Ueber Hyalitis und Cyclitis, Arch. f. Ophth. **86**:1-68, 1913.

33. Goulden, C.: Inflammation of the Uveal Tract Secondary to Infection of Mucous Membranes, Roy. London Ophth. Hosp. Rep. **19**:328-375, 1914.

34. Irons, E. E., and Brown, E. V. L.: The Etiology of Iritis, J. A. M. A. **81**:1771-1776 (Nov. 24) 1923.

35. Bulson, A. E.: The Etiology and Treatment of Endogenous Iritis: An Analysis of One Hundred Consecutive Cases in Private Practice, Tr. Am. Ophth. Soc. **23**:292-327, 1925.

5 per cent of 100 cases; Gilbert,[36] in 3 per cent of 500 cases; Gifford,[37] in 7 per cent of 118 cases, and Zeeman,[38] in 12 per cent of 290 cases.

In a series of 562 patients with uveitis, Guyton and Woods[39] expressed the belief that gonorrhea was the definite etiologic factor in 1.8 per cent and the presumptive etiologic factor in an additional 2.8 per cent. While admitting that the criteria for the gonorrheal origin of a particular case of uveitis were open to criticism and left doubt as to the accuracy of the diagnosis, they stated that the "complement fixation test is of principal value in ruling out the possibility of gonorrhea as a cause of uveitis."

In this connection, it might be well to heed the warning of some acknowledged experts in the general field of gonorrhea. Van Slyke, Thayer and Mahoney[40] stated: "There is a distinct tendency to ascribe to laboratory findings a degree of infallibility which may exceed the limitations of the procedure employed." Their findings are worth summarizing. Cultures and duplicate smears were made of the cervical secretion of 664 female patients. One hundred and forty of the cultures were found to yield gonococci, the identity of the organisms being confirmed in all instances by appropriate sugar fermentation reactions. The smears for these 140 patients were examined by three competent microscopists and reported to show gonococci in 88, 47 and 40 instances, respectively. The smears for the 524 patients with negative cultures for gonococci were reported by the same three microscopists to contain the organisms in 76, 13 and 4 instances, respectively.

With such inconsistency in the bacteriologic diagnosis of an easily accessible genital type of gonococcic infection, it is no wonder that a positive diagnosis of intraocular gonorrhea can so rarely be established.

The gonococcus complement fixation test has been disappointing as a diagnostic procedure. As a result of several studies, its validity has been seriously questioned. Göhring,[41] for example, in a comparative series of complement fixation tests made on 300 patients with gonorrhea, found positive reactions in 42 and 51 per cent, respectively, when two different gonococcus antigens were used and in 40 per cent when a

36. Gilbert, W., in Schieck, F., and Brückner, W.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 5, p. 3.

37. Gifford, S. R.: A Review of the Literature on the Etiology of Acute Iritis, Am. J. Ophth. **14**:100-110, 1931.

38. Zeeman, W. P. C., in Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 634.

39. Guyton, J. S., and Woods, A. C.: Etiology of Uveitis: A Clinical Study of Five Hundred and Sixty-Two Cases, Arch. Ophth. **26**:983-1018 (Dec.) 1941.

40. Van Slyke, C. J.; Thayer, J. D., and Mahoney, J. F.: Comparison of Media and Laboratory Results in Gonococcus Cultures, Am. J. Syph., Gonor. & Ven. Dis. **26**:55-62, 1942.

41. Göhring, G.: Experimentelle Untersuchungen zur Komplementbindungsreaction bei Gonorrhoe, Dermat. Wchnschr. **111**:625-628, 1940.

staphylococcus antigen was used. He also found a change in the reactions of the gonococcus complement fixation test in human subjects from negative to positive on the intravenous injection of suspensions of killed meningococci or staphylococci in increasing doses. In a recent critical review, Thomas [42] concluded that the complement fixation test for gonorrhea was not sufficiently accurate to have gained wide acceptance.

The application of sulfonamide compounds and of penicillin to the therapy of gonorrhea has in general constituted a great step forward. However, sulfonamide-resistant gonorrhea has become common, and more recently it has been demonstrated that the gonococcus may become resistant to penicillin.[43] The problem of gonorrhea is by no means completely overcome.

## REVIEW OF THE LITERATURE ON EXPERIMENTAL GONORRHEAL IRITIS

The gonococcus has been a notably difficult organism to study in experimental infection. In an extensive survey of the literature from 1786 to 1943, Hill [44] was able to report little in the way of positive results. In the 234 papers she reviewed, no experiments were successful which utilized genitourinary tissue, rectal mucosa, nasal mucosa, pleura, joints, skin and subcutaneous tissues, the central nervous system, or the circulatory system as sites of the infection. A generalized sepsis has been produced in mice by means of peritoneal injection,[45] but this does not meet the needs of problems which require a localized infection for their investigation.

In a large number of the studies reviewed by Hill, ocular tissues were utilized. An occasional observer reported the presence of gonococci after conjunctival inoculation, particularly after sensitizing the tissue with bile; but the results all too often could not be confirmed or were marred by the presence of secondary contaminants. Corneal and subconjunctival inoculation gave similarly disappointing results.

Risso,[46] in 1892, on the injection of a suspension of organisms into the anterior chamber of the guinea pig, noted clouding of the aqueous after twenty-four hours and was able to see intracellular diplococci in the fluid.

---

42. Thomas, R. B.: The Gonococcus and Gonococcal Infections, Am. J. Syph., Gonor. & Ven. Dis. **26**:691-774, 1942.

43. Bahn, J. M.; Ackerman, H., and Carpenter, C. M.: Development in Vitro of Penicillin-Resistant Strains of the Gonococcus, Proc. Soc. Exper. Biol. & Med. **58**: 21-24, 1945. Miller, C. P., and Bohnhoff, M.: Studies on the Action of Penicillin: IV. Development of Penicillin Resistance by Gonococcus, ibid. **60**:354-356, 1945.

44. Hill, J. H.: Experimental Infection with Neisseria Gonorrhoeae: II. Animal Inoculations, Am. J. Syph., Gonor. & Ven. Dis. **28**:334-378 and 471-510, 1944.

45. Miller, C. P., and Hawk, W. D.: Experimental Gonococcal Infection, Tr. A. Am. Physicians **55**:216-218, 1940.

46. Risso, A.: Colture del gonococco a scopo clinico, Riforma med. **8**:507-509, 1892.

Steinschneider,[47] in 1893, noted that the injection of gonococci together with the medium (serum agar) into the anterior chamber of the rabbit was followed by the appearance of conjunctival hyperemia, clouding of the cornea, grayish white exudate in the anterior chamber and hypopyon. Both cultures and smears consistently failed to show gonococci. When either the gonococci or the medium alone was injected, no inflammatory reaction occurred.

De Christmas,[48] in 1897, reported the recovery of gonococci from the anterior chamber of the rabbit for twenty-four to forty-eight hours after inoculation. He defined the nature of the problem by stating that the gonococcus was not destroyed by the animal, "but dies principally because it does not find in the milieu of the living (laboratory) animal the conditions necessary for its survival. It is not known of what the particular conditions consist, or the specific properties of human mucosa which constitute so propitious an environment for this microbe, but the environmental differences must be important, since it appears thus far impossible to adapt the gonococcus to a new milieu."

Pompéani,[49] working in de Christmas' laboratory, inoculated the anterior chamber of rabbits with a bacteriologically sterile, alcohol-precipitated gonococcus toxin and noted a severe inflammatory reaction, manifested by chemosis, corneal opacification and vascularization, and hypopyon. He considered that this result demonstrated the remarkable pyogenic properties of the toxin. Intracorneal introduction of the toxin elicited the same results, as did injection of living gonococci. He also claimed to have produced a serum which was able to neutralize to a great extent the pyogenic action of the toxin.

Da Fonseca,[50] in 1898, inoculated the anterior chamber of the rabbit and observed some corneal opacification, hypopyon, anterior and posterior synechias and pupillary membranes. The inflammatory response diminished at the end of a week. Microscopic studies showed active phagocytosis, to which he ascribed the absence of gonococci in cultures of material obtained by the second day.

Scholtz [51] inoculated the anterior chamber of the rabbit with small numbers of living or killed gonococci and observed diffuse suppuration in the anterior chamber and clouding of the iris within a few hours. The

47. Steinschneider: Ueber die Cultur der Gonokokken, Berl. klin. Wchnschr. **30**:728-731, 1893.

48. de Christmas, J.: Contribution a l'étude du gonocoque et de sa toxine, Ann. l'Inst. Pasteur **11**:609-639, 1897.

49. Pompéani, F.: Toxine et antitoxine du gonocoque, Thesis, Paris, no. 170, Guerin, Derenne et Cie, 1898.

50. da Fonseca, A. R.: Contribuição para o estudo do gonococco, Coimbra med. **18**:324-327, 384-387, 393-395 and 414-416, 1898.

51. Scholtz, W.: Beiträge zur Biologie des Gonococcus (Cultur, Thierexperimente und klinische Beobachtungen über gonococcenhaltige Abscesse im Bindegewebe), Arch. f. Dermat. u. Syph. **49**:3-28, 1899.

pus was always sterile. He concluded that the inflammatory response was chemotoxic in origin.

Maslovski,[52] in 1899, injected three day serum broth cultures into the anterior chamber of 10 rabbits and obtained identical results in all the animals. At the end of one day there was diffuse corneal opacification and pus was beginning to accumulate in the anterior chamber. The pus contained polymorphonuclear leukocytes without gonococci. Numerous colonies of gonococci were obtained on culture after twenty-four hours, fewer after forty-eight hours and none on the third day.

Cantani,[53] in 1899, reported conjunctival and corneal inflammation, regressing after four days, on intraocular inoculation of a rabbit with gonococci. Culture of the mucopurulent secretion from the conjunctiva yielded no organisms.

Bruck,[54] in 1909, cited work performed with Meirowski in which gonococci were injected into the anterior chamber of the rabbit. Living gonococci were recovered after forty-eight hours, but not after seventy-two hours, when the inflammation subsided and absorption and organization of the exudate commenced. He expressed the belief that the process was not at all specific for the gonococcus.

Debré and Paraf,[55] in 1913, aspirated aqueous from the anterior chamber of the rabbit and then injected a suspension of gonococci containing approximately 200,000,000 to 300,000,000 organisms. A severe purulent panophthalmitis developed, progressing in some instances to corneal perforation. It resolved in about a month and was followed by atrophy of the bulbus. No microscopic or cultural studies were made.

Mezincescu and Holban,[56] in 1919, following up the work of Debré and Paraf, were unable to find or to culture organisms. Since they were able to elicit similar suppuration on the inoculation of killed gonococci, they concluded that the reaction was a purely toxic one and that the gonococcus was not pathogenic for laboratory animals.

---

52. Maslovski, V. I.: Le role de la toxine du gonocoque dans les infections gonorrheiques des organes génitaux internes de la femme, Ann. de gynéc. et d'obst. **52**:574-588, 1899.

53. Cantani, A.: Contributo allo studio del gonococco, Riforma med. **15**:808-810, 819-821 and 831-833, 1899.

54. Bruck, C.: Ueber spezifische Behandlung gonorrhoischer Prozesse, Deutsche med. Wchnschr. **35**:470-474, 1909.

55. Debré, R., and Paraf, J.: Bases expérimentales de la sérothérapie antigonococcique: I. Ophthalmie expérimentale du lapin; son traitment par un serum specifique, Compt. rend. Soc. de biol. **75**:512-514, 1913; Principes généraux et bases expérimentales de la sérothérapie antigonococcique, Presse méd. **21**:1013-1015, 1913.

56. Mezincescu, D., and Holban, D.: Sur l'ophthalmie expérimentale à gonocoque chez le lapin, Comp. rend. Soc. de biol. **82**:536-537, 1919.

Terrien, Debré and Paraf,[57] in 1920, reported on further work done by their group, describing the ophthalmia in greater detail, together with histologic studies. The usual result of inoculating the anterior chamber of the rabbit with gonococci was a torpid iridocyclitis, evolving in ten to fifteen days, with moderate pericorneal injection, a large amount of exudate in the anterior chamber, synechias and abundant pus in the anterior chamber, terminating in total occlusion of the pupil and partial clouding of the cornea. In a few cases the involvement was less severe, with slight pericorneal injection, few synechias and little or no hypopyon. In other cases the involvement was graver, with severe pericorneal reaction, a much larger accumulation of pus in the chamber, glaucoma and sometimes corneal perforation and phthisis. They produced drawings of the histologic changes in the involved eyes but said nothing about searching for gonococci, either in the sections or by cultural methods. They merely cited Morax to the effect that gonococci did not grow in the observed lesions, apparently referring to the paper by Morax and Elmassian,[58] in which the statement was made that gonococci did not grow in or on animal conjunctivas on inoculation of the living microorganisms.

Cohn,[59] in 1931, made the most noteworthy recent contribution. He injected a turbid suspension of gonococci in isotonic solution of sodium chloride or Ringer's solution into the anterior chamber of the rabbit. He likened the clinical appearance of the eyes to that of similarly affected human eyes; with conjunctivitis, pericorneal injection, corneal opacification, and exudate and pus in the anterior chamber. These changes were present in one or another combination after twenty-four hours, became more intense during the following days and remained unchanged thereafter for three to four weeks. Cohn utilized twelve strains and a mixture of strains of the gonococcus in a total of 54 experiments. Material for culture was obtained by aspiration of the aqueous. Of the 54 cultures, the gonococcus was found in 21 between the fourth and twenty-eighth day. Some strains in particular yielded positive cultures in a significantly greater proportion of inoculations than did others. He concluded:

> The injection of gonococci in the anterior chamber of the rabbit causes local clinical signs, but the viability of the infecting agent in the individual animal is variable and irregular. It is, nevertheless, noteworthy that in 2 instances gonococci were still culturally demonstrable after thirteen and twenty-eight days, respectively.

57. Terrien, F.; Debré, R., and Paraf, J.: Etude expérimentale sur la sérothérapie antigonococcique, symptômes et lésions de l'iridochoroïdite gonococcique, Arch. d'opht. **37**:326-343, 1920.

58. Morax, M., and Elmassian, M.: Du role des toxines dans la production des inflammations de la conjonctive, Ann. d'ocul. **122**:81-113, 1899.

59. Cohn, A.: Verimpfung von Gonokokken auf Kaninchen, Dermat. Ztschr. **60**:35-41, 1931.

This is something never previously observed in any animal experiment. All in all, it remains questionable whether the anterior chamber of the rabbit is suitable for experimental induction of gonorrhea.

Balsamelli [60] utilized the technic of Terrien, Debré and Paraf in studies on the effect of various gonococcic antiviruses. He noted the development of panophthalmitis and obtained gonococci in pure culture from such inoculated eyes; he concluded, therefore, that the gonococcus was pathogenic for the rabbit.

## EXPERIMENTAL PROCEDURE AND RESULTS

The work to be described here was originally initiated at the request of the Subcommittee on Venereal Diseases of the National Research Council as part of a comprehensive investigation into the whole problem of the chemoprophylaxis of venereal diseases. Its object was the development of methods for the testing of gonococcidal agents in vivo, which made it necessary to find a means of producing a localized gonococcic infection experimentally in some suitable laboratory animal.

These studies promised to yield results which bore not only on their primary objective but also on some of the many unsolved problems associated with uveitis. Preliminary [61] and final [62] reports on the study as a whole have already been published; to these the reader is referred for such details of technic as are beyond the scope of this paper, as well as immunologic, prophylactic and therapeutic observations.

The rabbits were healthy, young adults. Albinos were preferred, but it was not always possible to obtain them in sufficient numbers. Two strains of gonococci were used. One was derived from the blood culture of a patient with bacterial endocarditis; the other was from a patient with gonorrheal urethritis which had been resistant to sulfathiazole therapy. The medium used was a casein-digest cystine agar, usually enriched with 10 per cent fresh defibrinated rabbit blood. The cultures were incubated in a candle jar.

The rabbits were anesthetized with morphine or "demerol hydrochloride" (meperidine hydrochloride) intravenously and solution of cocaine or tetracaine topically. The hair around the eyes was clipped, and the lids were held apart with a speculum. Two-tenths cubic centimeter of aqueous was aspirated from

60. Balsamelli, F.: Ricerche sperimentali sull'azione degli antivirus specifici ed aspecifici sul gonococco, Boll. d. Ist. sieroterap. milanese **13**:420-426, 1934; Propriete immunizanti e terapeutiche degli antivirus specifici ed aspecifici nell'ipopion gonococcico sperimentale del coniglio, ibid. **14**:232-236, 1935.

61. Miller, C. P.; Moeller, V., and Bohnhoff, M.: A Method for Production of a Localized Gonococcal Infection in the Rabbit's Eye, Proc. Soc. Exper. Biol. & Med. **58**:143-146, 1945.

62. (*a*) Miller, C. P.; Drell, M. J.; Moeller, V., and Bohnhoff, M.: Experimental Gonococcal Infection of the Rabbit's Eye: I. Method of Production, J. Infect. Dis. **77**:193-200, 1945. (*b*) Drell, M. J.; Miller, C. P.; Bohnhoff, M., and Moeller, V.: Experimental Gonococcal Infection of the Rabbit's Eye: II. Course of the Disease and Its Pathology, ibid. **77**:201-215, 1945. (*c*) Miller, C. P.; Bohnhoff, M., and Moeller, V.: Experimental Gonococcal Infection of the Rabbit's Eye: III. Treatment with Prophylactic and Therapeutic Agents, ibid. **77**:216-223, 1945.

the anterior chamber by means of a 25 or 26 gage hypodermic needle fitted to a tuberculin syringe. With a second syringe and needle, 0.2 cc. of a suspension of gonococci in saline solution was then injected through the same needle track into the anterior chamber.

During the procedure the anterior chamber was emptied, and in many instances the hypodermic needle was observed to have inflicted trauma on the iris or the lens or both. Accordingly, in later phases of the investigation, a single syringe-puncture technic was used. The needle attached to a syringe containing the suspension of gonococci was introduced through the cornea into the anterior chamber. By repeated partial aspirations and injections a thorough mixture of the suspension of gonococci and the aqueous was effected, the anterior chamber contents at no time being more than half evacuated. The chamber was then completely filled and the needle withdrawn. The heat of summer was found to reduce the percentage of infections induced, and so the animals were kept in a room artificially chilled to a temperature of 50 to 60 F.

The eyes were examined grossly and studied with an ophthalmoscope and a hand slit lamp at daily to weekly intervals. The tension was estimated by touch and with a Souter tonometer. Aqueous was withdrawn for culture, after anesthesia, with a syringe and hypodermic needle. At the end of the period of observation, the animals were killed by induction of air embolism. The bulbs were enucleated. Then either the several parts of the eyes were dissected under sterile conditions and streaked out on a culture plate or the bulbs were fixed in "Zenker-formol" (Zenker's fluid made up with solution of formaldehyde U.S.P.), embedded in paraffin, sectioned and stained with hematoxylin–eosin–azure II stain. In one series, an iridectomy was performed at the time of enucleation, the excised iris tissue cultured, and the rest of the bulb sectioned; this method yielded no gonococci in cultures, although the organisms could at times be identified in the sections. Attempts were made to preserve the morphologic character of the gonococci in the histologic sections by fixation with solid carbon dioxide immediately after enucleation; this was unsatisfactory. Some sections were stained with a modified Gram stain; this, too, was unsatisfactory.

Cultures from different parts of an eye were not uniformly consistent. The culture from one of its tissues sometimes yielded a heavy growth of gonococci, while that from another part of the same eye contained few colonies or none. In general, cultures from the anterior surface of the lens most frequently contained the largest number of gonococci; those from the ciliary body came next, and those from the aqueous and the vitreous humors third and fourth, in order of decreasing incidence. In fact, cultures from the vitreous so seldom yielded the gonococcus as to be insignificant. In most of the experiments time did not permit total excision of the ciliary body and adequate maceration by grinding. If a culture from any part of an eye contained gonococci, that eye was regarded as infected at the time of its enucleation.

In the microscopic sections, gonococci stained a darker blue than the corneal tissues and were more easily seen in those edematous tissues which stained more lightly. Typical pairs could sometimes be seen, although more commonly the two halves were not in the same plane. Not uncommonly, especially in the cornea, no gonococci of the usual morphologic character were seen. Instead, larger blue, globoid bodies,

sometimes apparently single, at other times paired, were observed. Since these bodies were seen only in eyes grossly similar to those yielding heavily positive cultures, it was felt that they represented degenerating, partially autolyzed, organisms. The gonococci appeared to be extracellular almost as often as they were intracellular. Not all the rabbits were albinos, and the intraocular pigment was sometimes confusing; with the hematoxylin-eosin-azure stain, however, the pigment had a definite dark brown color and was easily distinguished from the dark blue of the gonococci with the higher powers of the microscope. Nodal points in the fibrinous exudate often resembled gonococci; when fibrin was seen in the immediate or the intermediate vicinity, therefore, no organism was called a gonococcus unless it was quite typical. On the whole, then, a number of factors prevented easy identification of the gonococci. Nevertheless, histologic study of eyes in groups of animals yielding positive cultures did reveal gonococci, while eyes of groups of animals with negative cultures showed none.

In order to determine whether mere survival of organisms or actual multiplication occurred in the anterior chamber, several series of eyes were inoculated with approximately 200,000 gonococci and enucleated at intervals up to twenty-four hours thereafter. The ocular contents were then macerated, serially diluted and cultured. The results showed that at the end of twenty-four hours a definite increase in the number of viable gonococci had occurred.

To estimate the number of gonococci required to infect, inoculations of various dilutions of the suspension of gonococci were made. The eyes were then cultured after twenty-four hours. Of 266 eyes inoculated with approximately 20,000,000 gonococci, the organisms were obtained on culture in 93 per cent; of 32 eyes inoculated with 2,000,000 gonococci, in 84 per cent; of 28 eyes inoculated with 200,000 gonococci, in 82 per cent; of 32 eyes inoculated with 20,000 gonococci, in 65 per cent; of 26 eyes inoculated with 2,000 gonococci, in 46 per cent; of 22 eyes inoculated with 200 gonococci, in 45 per cent, and of 10 eyes inoculated with 20 gonococci, in none. Thus, 200 organisms appeared to be the minimal infecting dose.

The most convenient criterion of the duration of infection was the length of time viable gonococci could be recovered from inoculated eyes. This was determined by inoculating a series of eyes with approximately $2 \times 10^7$ gonococci each and then killing the animals at regular intervals and making complete cultures of their eyes. The results showed that during the first week there was a progressive decrease in the percentage of eyes from which viable gonococci could be cultivated. At the end of the week slightly more than a third of the eyes were still infected. Thereafter, the proportion of infections with viable gonococci continued to be about the same, although the observations were made at longer intervals. These results indicated that the infection became

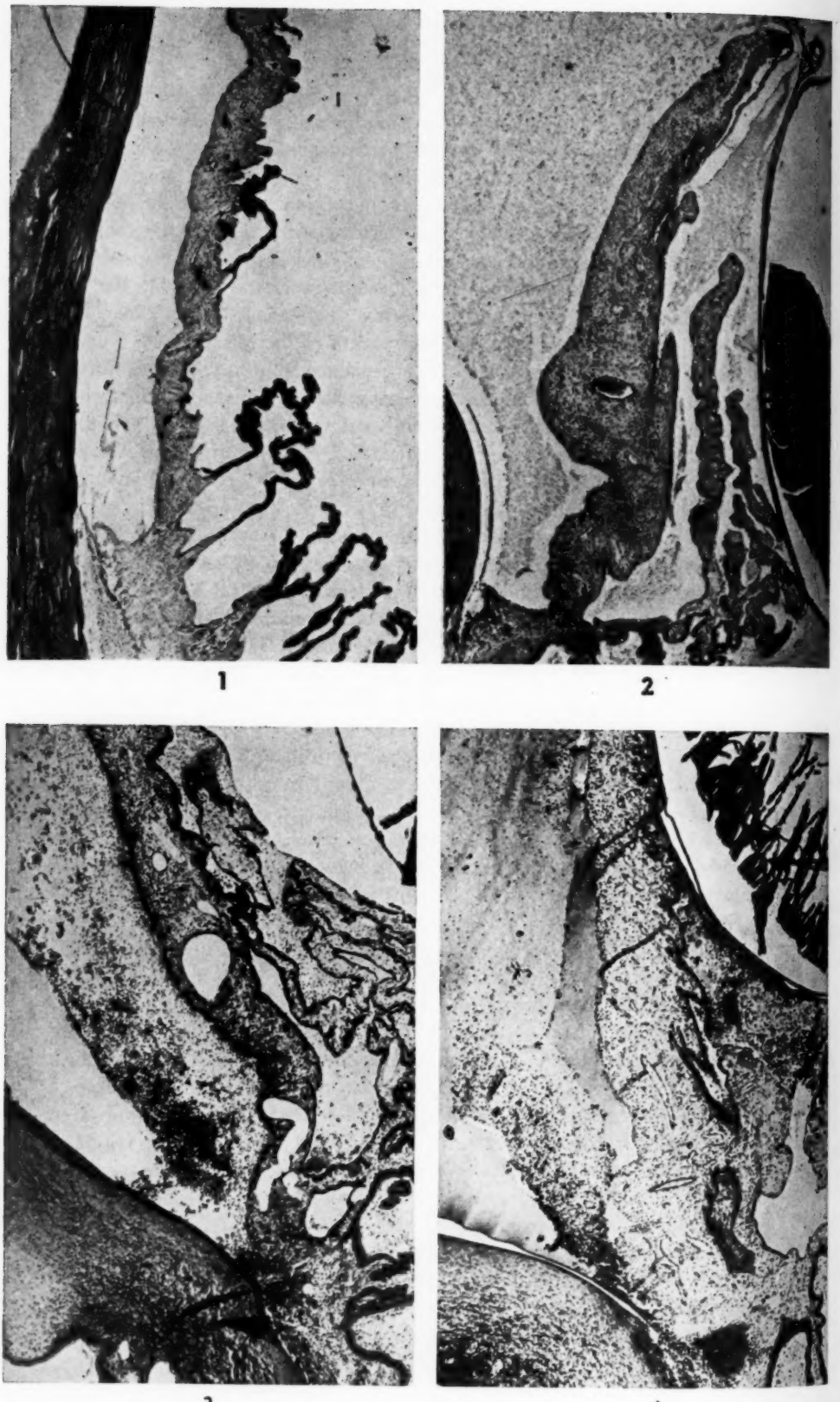



Figure 2

*(See legend on opposite page)*

chronic in approximately a third of the eyes and persisted for as long as fourteen weeks, the maximum period of observation.

Injection of sterile saline solution into the anterior chamber after aspiration of the aqueous resulted in slight conjunctival hyperemia with complete clinical recovery in a day. When enucleated after twenty-four hours, the eyes showed a slight fibrinous and noncellular exudate in the anterior chamber, with a few polymorphonuclear leukocytes enmeshed in the angle of the anterior chamber (fig. 2, *1, 2*).

Sections of eyes enucleated twenty-four hours after inoculation with gonococci (fig. 2, *3*) showed extensive fibrinous and cellular exudate. The exudate tended to form a layer overlying the iris. The cells were predominantly polymorphonuclear leukocytes, which, together with clumps of fibrin and debris, filled the meshwork of the angle of the chamber. Similar sections from eyes a week after inoculation showed relatively few leukocytes in the anterior chamber. The ciliary body was at times infiltrated with polymorphonuclear leukocytes and relatively more round cells than in the eyes at twenty-four hours (fig. 2, *4*). In other eyes the picture was that of a quickly subsiding acute inflammatory process with a few signs of permanent or residual change (fig. 3, *5*). Many bodies resembling gonococci were to be seen, but none which was typical.

In another series of 38 rabbits, the eyes were inoculated and observed for periods of two to fourteen weeks. Repeated cultures of the aqueous humor and agglutination and complement fixation tests on the serum were made, as well as cultures of the lens and ciliary body at autopsy. The results are reported in detail elsewhere.[62b] In 49 of the 76 eyes gonococci were recovered at some time during life or at autopsy; in 27 of the 76 eyes they were not. In 18 of the eyes gonococci were demonstrated at some time during life but not at autopsy; in 10 of the eyes gonococci were cultivated for the first time at autopsy.

Since the study of this series of eyes was virtually completed before the significance of the appearance of the inoculated eyes was appreciated, another, but smaller, series was initiated and studied with this point in mind. This series comprised the 22 eyes of 11 rabbits. Inoculation was effected by the modified method, requiring only a single needle

---

Fig. 2.[62]—Photomicrographs, showing the angle of the anterior chamber and its surroundings; × 32. *1*, normal eye. The lens fell out during sectioning. *2*, twenty-four hours after injection of isotonic solution of sodium chloride. Note the curled, torn capsule of the lens, indicating that it had been injured during injection. The iris and ciliary processes were moderately edematous. Slightly fibrinous, noncellular exudate was present in the anterior chamber. *3*, twenty-four hours after inoculation with gonococci, showing moderate fibrinous exudate with many polymorphonuclear leukocytes. *4*, one week after inoculation with gonococci. Note the moderate number of leukocytes in the contracting fibrinous exudate. A heavy focal polymorphonuclear and lymphocytic infiltration, together with some gonococci, was present at the root of the iris.

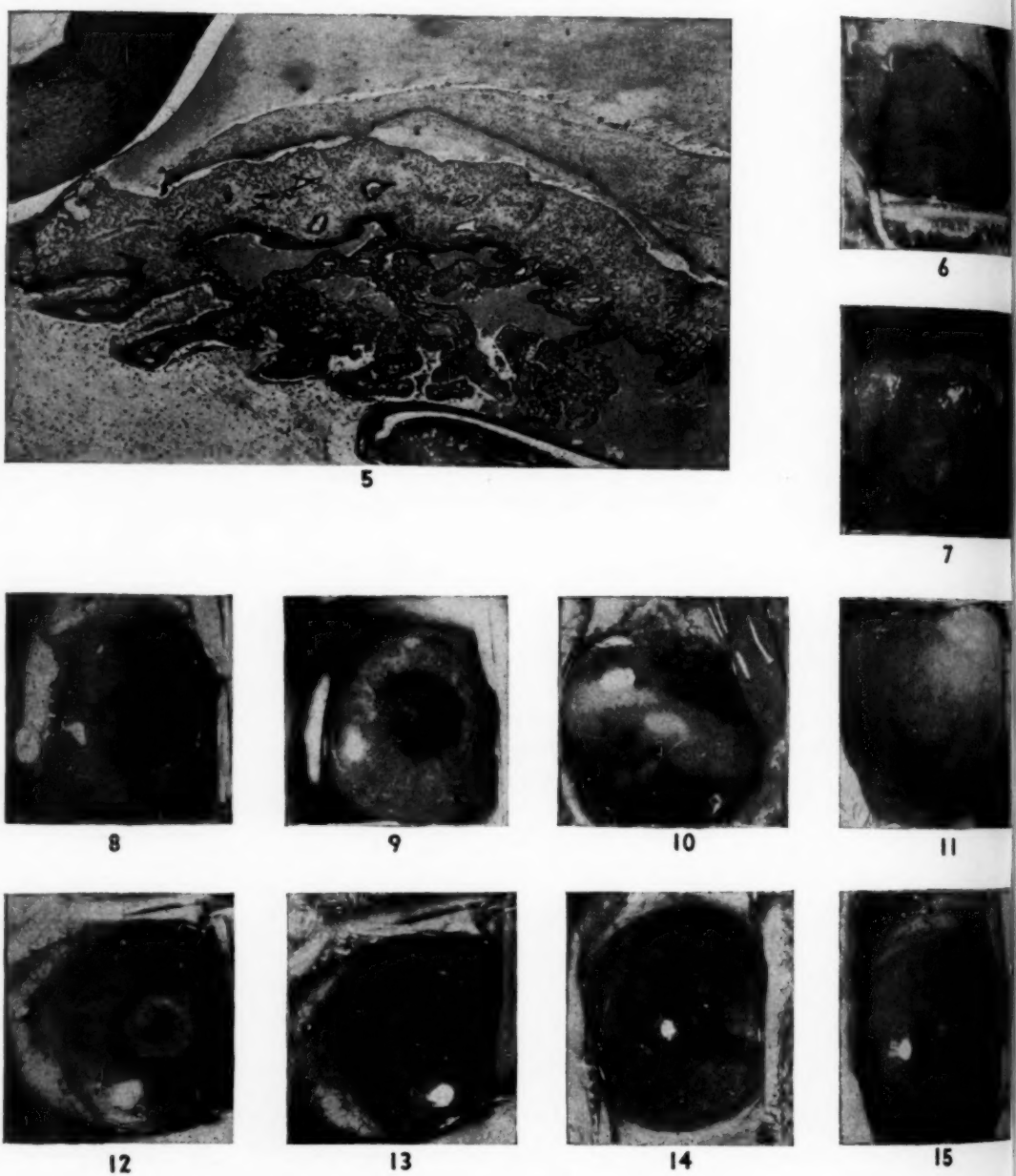



Figure 3

*(See legend on opposite page)*

puncture. The second of the two strains of gonococcus was used. In 6 of the rabbits the lenses were deliberately torn by the hypodermic needle at the time of inoculation; these eyes will be referred to, hereafter, as "injured." In the other 5 rabbits, sufficient care was taken to make reasonably certain that the lenses were not injured; these eyes will be referred to as "uninjured."

The table shows the results of postmortem examinations for gonococci in this series. The eyes were observed every two to seven days over a period of two to five weeks. The 12 injured and the 10 uninjured

*Bacteriologic and Histologic Demonstration Post Mortem of Gonococci in Rabbit Eyes*

| | Injured Eyes | | Uninjured Eyes | |
|---|---|---|---|---|
| Number of eyes cultured | 6 | | 5 | |
| Number of eyes yielding gonococci on culture | | 5 | | 0 |
| Number of eyes examined histologically | 6 | | 2 | |
| Number of eyes showing gonococci histologically | | 5 | | 0 |
| Total number of eyes | 12 | | 7* | |

* Three other uninjured eyes were apparently normal and were neither cultured nor sectioned.

eyes were then enucleated; 1 eye of each rabbit was cultured and the other prepared for histologic study. It was later regretted that 3 of the uninjured eyes, although they were to all appearances completely normal at the time of killing the animal, were neither cultured nor sectioned.

Fig. 3.[62]—*5*, angle of the anterior chamber and surroundings one week after inoculation with gonococci; × 32. A mild, relatively noncellular residual inflammation was present. *6*, eye 47L of figure 4, two days after inoculation with gonococci. The lens was not traumatized. The cornea was moderately opaque. A heavy generalized exudate was present in the anterior chamber. *7*, same eye as that shown in *6*, on the eighth day after inoculation. The membrane was dense but was localizing to the pupillary space. Some vessels were present in the cornea. *8*, same eye, on the twenty-first day. The exudate was still more shrunken and adherent to the lens. Vessels persisted in a single sector of the cornea. *9*, same eye, on the thirty-sixth day. The cornea was normal. Residual membrane was adherent to the anterior surface of the lens, with posterior synechias. *10*, eye 48L of figure 4, four days after inoculation with gonococci. The lens was not traumatized. A moderately heavy exudate was present in the anterior chamber. Moderate vascularization was present at the periphery of the cornea. *11*, eye 44R of figure 4, twenty-one days after inoculation with gonococci. The lens was traumatized. The cornea was deeply opaque, rough and vascular. *12*, eye 48R of figure 4, four days after inoculation with gonococci. The lens was not traumatized. A moderately heavy membrane protruded into the anterior chamber from behind and around the pupillary margin. *13*, same eye as that shown in *12*, on the eighth day after inoculation. The membrane was considerably smaller and thinner. *14*, eye 43R of figure 4, eight days after inoculation with gonococci. The lens was traumatized. The pupil was slitlike. *15*, eye 42L of figure 4, twenty-one days after inoculation with gonococci. The lens was traumatized. The pupil was piriform, with anterior and posterior synechias.

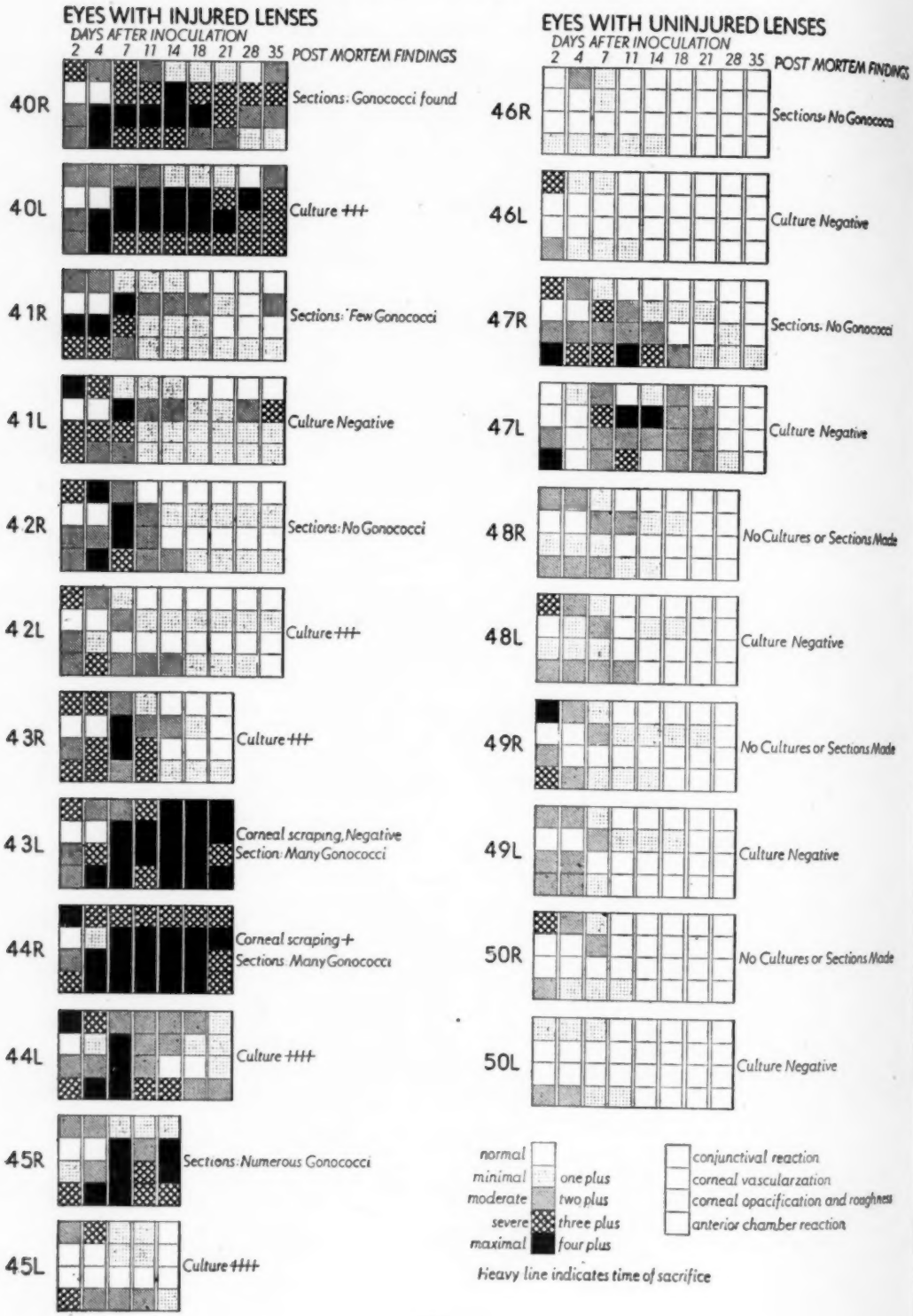



Figure 4

*(See legend on opposite page)*

From 2 of the injured eyes some of the superficial corneal tissue was scraped and cultured at the time of enucleation. One of these 2 cultures yielded gonococci. The 2 eyes were subsequently studied histologically; both showed numerous gonococci in the sections.

Figure 4 shows in graphic form the course of the infection in each of the eyes of this series. The observations were divided into four categories: conjunctival reaction; corneal vascularization; corneal roughness and opacification, and reaction of the anterior chamber (fig. 3, *6* to *15*).

The conjunctival reaction included conjunctival discharge, hyperemia and chemosis. A serous or mucoid conjunctival discharge was noted in all eyes on the first few days after inoculation. It was slightly more profuse in the injured eyes. By the end of the first week it had almost completely subsided. Repeated cultures of the discharge yielded no gonococci. Conjunctival hyperemia, seen in all the eyes, reached its maximum during the middle of the first week and was severer in the injured eyes. It disappeared in the uninjured eyes by the end of the week but persisted until the eighteenth day in a majority of the injured ones. Chemosis was present in all eyes for several days after inoculation; no difference was noted between the two groups. The recurrence of the conjunctival reaction in 2 of the injured eyes during the final week of study represented a change associated with the development of glaucoma and staphyloma in those 2 eyes.

Corneal vessels (fig. 3, *10*) began to grow inward from the periphery at about the end of the first week in all eyes. This process was generally much severer in the injured eyes, varying from a slight peripheral vascularization, in the corneas which were transparent, to extensive vascularization of all but the vertex, in the corneas which were rough and opaque. During the third week the vascularization in the uninjured eyes, never severe, began to recede, whereas that of the injured eyes remained much the same.

Corneal opacification developed in 6 of the uninjured eyes. Four of these eyes cleared up within eleven days; the other 2 remained opaque until the twenty-first day, and severe roughness of the corneal surface developed during this period. Corneal opacity was present in all the injured eyes, reaching its maximum at the end of the first week; the opacity assumed a deeply crackled appearance, like isinglass, and was associated with roughness of the surface in 10 of the 12 eyes. Clearing of the corneas then began, although more than half the eyes remained opaque to some extent until the end of the study (fig. 3, *11*).

---

Fig. 4.[62]—Diagrammatic representation of the changes observed during the course of gonococcic infection in eyes with injured and with uninjured lenses. In each block, the top row of squares indicates conjunctival reaction; the second row, corneal vascularization; the third row, corneal opacification and roughness, and the bottom row, reaction of the anterior chamber.

The reaction in the anterior chamber consisted of a grayish white, milky exudate in all the eyes during the first week and was greatest about the middle of the week. In those eyes in which the corneas were sufficiently clear to make observation possible, the exudate seemed to be curling forward into the anterior chamber around the pupillary margin from behind the iris (fig. 3, *12* and *13*). A small hypopyon was present in some of the uninjured eyes. During the second week the exudate condensed to a heavy white membrane, which by the end of that week had disappeared in all but 1 eye. In the injured eyes the corneal changes rendered observation of the anterior chamber more difficult. The exudate, however, was considerably heavier, and a large hypopyon was present in most of the eyes, persisting until the end of the study in one fourth of them. In some a layer of hemorrhage overlay the hypopyon. All the irises showed a variable, but generally severe, vascular engorgement. In the later stages, in the uninjured eyes, evidences of atrophy of the iris appeared. Formation of synechias, both anterior (iris to posterior surface of cornea) and posterior, led to abnormal pupillary shapes (fig. 3, *14, 15*). Virtually all the uninjured eyes had assumed a normal appearance by the fourth week. This was not the case in the injured eyes.

The intraocular tension was elevated for a short period in 2 of the uninjured eyes. It was elevated in 1 injured eye on a single occasion during the second week; in 2 other injured eyes, both of which became staphylomatous, the tension was persistently elevated from the eleventh to the thirty-fifth day. Eyeballs similarly studied, though not included in this particular series of observations, have been found to have ruptured on occasion.

It should be noted here that some of the eyes observed during this study, though not in this series, showed pseudogliomatous masses in the vitreous. No chorioretinitis was observed at any time, and it appears unlikely to have occurred, since the histopathologic changes essentially were those of anterior uveitis. Optic neuritis was looked for but was not seen at any time. Some of the eyes appeared to have posterior subcapsular polychromatic opacities of the lens, of the kind typically seen in association with inflammations of the posterior segment (Bellows[63]), although the pathologic process appeared to be confined to the anterior segment.

Histologic sections were made of 6 injured and 2 uninjured eyes.

In the uninjured eyes the following features were apparent: The cornea was normal or showed only an occasional obliterated blood vessel with slight cellular infiltration surrounding it. The anterior and posterior chambers contained no fibrin and few cells. The angle of the

63. Bellows, J.: Cataract and Anomalies of the Lens, St. Louis, C. V. Mosby Company, 1944, pp. 378-384.

chamber was normal. The iris and the ciliary body were mildly infiltrated with round cells and were not engorged (fig. 5, *16*). The ciliary processes were virtually normal.

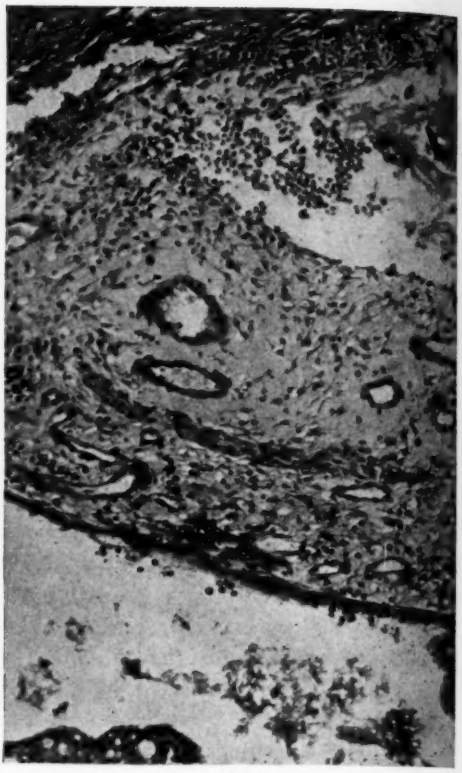
The eyes with injured lenses, on the other hand, showed numerous and more extensive changes (fig. 5, *17*): The cornea was thickened, in some instances two or threefold. It was infiltrated with numerous polymorphonuclear leukocytes as well as macrophages. Vascularization was clearly evident; in addition to large vessels superficially placed near the corneal periphery many fine vessels, down to those of capillary caliber, were seen throughout all the layers of the stroma (fig. 5, *18*). The stroma itself stained poorly. Gonococci, both typical and degenerating forms, could be distinguished intracellularly and extracellularly in the cornea. The anterior chamber contained varying amounts of fibrinous exudate, together with normal and degenerating leukocytes and some gonococci, all of which formed heavy accumulations on the iris and adjacent to the angle of the anterior chamber. Collections of fibrin and leukocytes were adherent to the posterior surface of the cornea (keratic precipitates); no definite gonococci could be identified in these areas. The meshwork of the angle of the chamber was filled with leukocytes and gonococci (fig. 5, *19*). In 2 eyes in which sections showed the site of the injury to the lens there occurred a thick membrane, consisting of fibrin and fibroblasts, as though an attempt had been made to seal off the torn capsule of the lens; within this membrane gonococci, closely associated with rounded morgagnian globules of degenerating lens material, were particularly numerous. The iris and the ciliary body showed a variable, but on the whole moderate to severe, inflammatory reaction; an occasional gonococcus could be distinguished in the iris. The ciliary processes in the more severely involved eyes were greatly edematous, covered with an albuminous exudate and apparently adherent to the lens by means of this exudate. In 1 case the cornea was grossly ectatic. The lenses were not well preserved during the process of sectioning and fell out in some instances, while shreds of lens fibers were scattered throughout the section in others. Except for slight choroidal engorgement and slight cellular infiltration (artefact?) in the vitreous, the posterior segment of the eye was normal.

## COMMENT

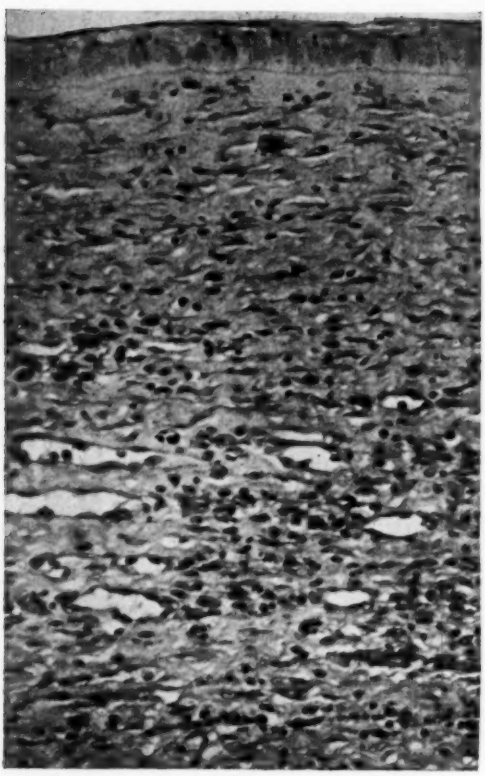
The gonococcic infection experimentally induced in the rabbit eye was a true infection. Proof of this was the evidence of multiplication of the organisms and their recovery on culture.

The appearance of the experimental infection was similar to that in some cases of human gonorrheal iritis. The gelatinous exudate, the intense iridic engorgement and the hypopyon and hyphema were virtually reproduced. Histologically our observations were in close agreement with those of Byers and Velhagen. The curling forward of the exudate into

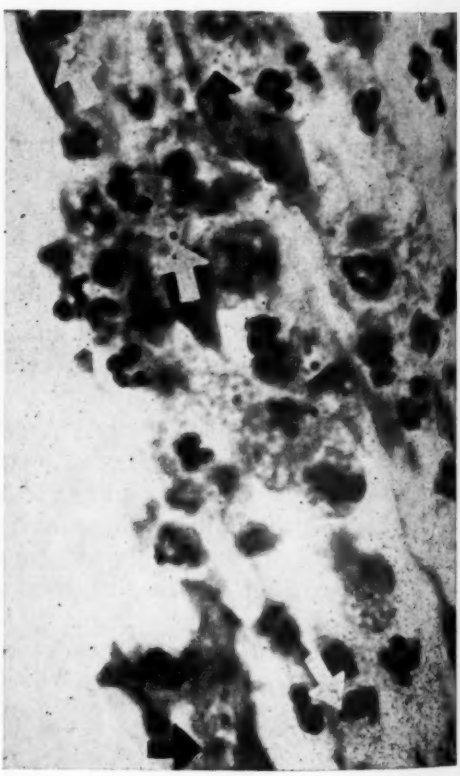
16



17



18



19

**Figure 5**

*(See legend on opposite page)*

the anterior chamber around the margin of the pupil from behind the iris probably represented the passage into the anterior chamber from the posterior chamber of the fibrinocellular exudate elaborated by the ciliary body.

The optic neuritis observed occasionally by clinicians in association with gonorrheal iritis has not been seen by us, although it must be admitted that in the more severely involved eyes details of the fundus could not be seen. Histologically, however, the inflammatory process appeared to be virtually confined to the anterior segment. The optic neuritis has been attributed by some authors to a toxic effect exerting its action backward from the anterior segment on the vulnerable optic nerve head. Just why the optic nerve head should be so vulnerable is not made clear. It would be just as rational to assume that gonorrheal iritis, occurring, as it does, in man as a metastatic manifestation of gonococcemia, can sometimes be accompanied with the additional metastatic involvment of the optic nerve.

Gonorrheal iritis in the past has been almost exclusively a disease of males. One possible reason for this—the instrumentation in treatment of gonorrhea in males, has already been pointed out. Another reason may be that gonorrhea in females, particularly in its chronic aspects, has only recently attained recognition.

An absolute diagnosis of gonorrheal iritis can rarely be made. The present knowledge of the immunologic reactions associated with gonorrhea is of little aid in this respect. Routine paracentesis of the anterior chamber is not ordinarily feasible; furthermore, experimentally, rabbit eyes from which the aspirated aqueous repeatedly yielded no growth on culture occasionally revealed a heavy growth of gonococci on postmortem culture of the ocular tissues. Bits of excised iris had even less value for the demonstration of viable gonococci; even histologically the gonococcus was recognized only with difficulty. Should enucleation be done in new cases of human gonococcic iritis, the eyes would certainly yield more important information if subjected to histopathologic study than if cultured for gonococci. Ordinarily, therefore, the diagnosis of gonorrheal iritis can be only a presumptive one.

---

Fig. 5.[62]—*16*, angle of the anterior chamber and surroundings of eye 46R of figure 4, thirty-five days after inoculation with gonococci; × 120. The lens was not traumatized. There was a mild residual cellular infiltration of the iris and the ciliary body. The anterior and posterior chambers were clear. *17*, angle of the anterior chamber and surroundings of eye 43L of figure 4, twenty-one days after inoculation with gonococci; × 125. The lens was traumatized. There was an extensive cellular exudate in the anterior chamber. The iris and ciliary processes were moderately edematous and infiltrated. *18*, portion of the cornea of the same eye as that shown in *17;* × 225. The cornea stained lightly and was greatly thickened, vascularized and infiltrated. Numerous gonococci were identified in this area. *19*, detail of the meshwork in the angle of the anterior chamber from *17;* × 1,1000 (oil immersion lens). Typical gonococci are indicated by black arrows; atypical gonococci, by white arrows.

The relation of injury to the lens, with its consequent liberation of lens protein, to the experimental iritis leads to interesting speculation. On the one hand, the lens, a protein-rich tissue similar to the mediums on which gonococci grow so easily, may be the single additional growth factor needed to foster multiplication of these micro-organisms in the otherwise suitable environment. On the other hand, the trauma of rupturing the capsule of the lens may be the factor which delays the normal reparative responses just enough to enable the micro-organisms to grow. The observation in the rabbit that the greatest proportion of positive cultures derives from the surface of the lens and the frequency with which gonococci are observed to be mixed with morgagnian globules tend to make the former hypothesis more acceptable than the latter, although the two are not necessarily mutually exclusive. Further work on this problem is the subject of another publication.[64]

The experimental infection lent itself well to in vivo testing of gonococcidal agents. For details of this work, the reader is referred to a previous paper.[62c] It may be mentioned here that, although relatively huge doses of systemically administered penicillin were required to control the experimental infection, as little as 2.5 units injected directly into the anterior chamber was able to do so.

Finally, gonorrheal iritis is a disease which can well bear more important consideration by ophthalmologists. The war-induced increase in the incidence of venereal diseases will probably lead to an increase in the incidence of their complications and sequelae, sulfonamide compounds and penicillin notwithstanding.

## SUMMARY

A technic for producing gonorrheal iritis in the rabbit eye is reported.

The percentage of eyes yielding cultures containing the gonococcus fell progressively during the first week after inoculation. Thereafter, the infection became chronic in about one third of the eyes. It seemed that injury to the lens was a major factor in making the infection chronic.

The eyes exhibited many of the gross appearances of human gonorrheal iritis. The histologic picture was initially that of an acute fibrinocellular response and later that of a chronic inflammatory process. The inflammation remained localized to the anterior segment of the eye.

Dr. Arlington C. Krause, of the Division of Ophthalmology, Department of Surgery, of the University of Chicago, gave aid in this study.

Figures 2, 3, 4 and 5 were originally published in the *Journal of Infectious Diseases* and are reproduced by permission of its editors and of its publisher, the University of Chicago Press.

1117 Second Avenue, Seattle.

950 East Fifty-Ninth Street, Chicago 37.

64. Drell, M. J.; Bohnhoff, M., and Miller, C. P.: The Role of Lens Substance in Experimental Gonorrheal Iritis, Am. J. Ophth. **29**:1263-1272, 1946.

# REPAIR OF ORBITAL DEFORMITIES WITH GLASS WOOL

ARTHUR GERARD DE VOE, M.D.
NEW YORK

Note has previously been made of the frequency with which depressed fractures of the orbital floor are associated with traumatic enophthalmos.[1] When the injury has been severe enough to necessitate removal of the globe, attempts at installing a satisfactory prosthesis are usually cosmetically unsatisfactory. The chief blemish is the loss of fulness normally present in the upper lid and its replacement by a disfiguring sulcus. To a less degree this defect is often seen after an uncomplicated enucleation and may possibly be due to atrophy of orbital fat associated with trauma incident to the operative technic. Particularly, when an attempt is made to secure a long stump to the nerve, the enucleation scissors may perforate Tenon's capsule and injure the blood supply to fat lobules.

It has been found that both types of defect may be remedied by the subperiosteal insertion of inert material in the floor of the orbit so as to restore the orbital volume to its original mass.[2] Many materials have been so used. These include autogenous and preserved cartilage, autogenous and preserved fascia lata, bone, tantalum wool, plates, ribbon and acrylic plates.

The purpose of this preliminary communication is to suggest a material which, so far as is known, has not been employed for this specific use. Glass has been used for many years for both immediate and delayed implants in the orbit. It has been well tolerated, its chief defect being the possibility of the glass sphere breaking. Further research by glass manufacturers has produced glass in many new forms. It has been made into yarn, wool and cloth, which have come to have certain applications in surgical procedures. Because of these uses, extensive investigations have been carried out to determine its toxicity for human tissues.[3] Increasing use of glass wool as an insulator, both

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology of the Presbyterian Hospital.

1. Pfeiffer, R. L.: Traumatic Enophthalmos, Arch. Ophth. **30**:718 (Dec.) 1943.

2. DeVoe, A. G.: Experiences with the Surgery of the Anophthalmic Orbit, Am. J. Ophth. **28**:1346, 1945.

electric and thermal, in industry has prompted scrutiny of the health of workers engaged in its production. Pneumoconiosis or other irritation to the lungs has not occurred. Glass wool, being composed of pure glass filaments, is nonabsorbent, is not affected by tissue fluids or enzymes, does not produce toxins or allergic reactions, is not susceptible to attack by bacteria and is not considered carcinogenic.[4] It has been used by dentists for packing root canals [5] and by surgeons as suture material [4] and, in the form of cloth, as dressings for direct application to burned surfaces.[6] It can be boiled or autoclaved indefinitely.

With these facts in mind, it was decided to use the material in fractures of the orbital floor. All other substances tried have presented some undesirable feature. The permanence of autogenous and preserved cartilage grafts is open to question. Bone must be autogenous and

Appearance (*A*) prior to and (*B*) after insertion of glass wool into the orbit.

requires a secondary operation for its procurement. Tantalum is heavy, radiopaque and subject to the development of high heat by induction should diathermy be inadvertently used. Certain patients are sensitive to acrylic compounds as they are presently made. In

3. Sulzberger, M. B., and Baer, R. L.: The Effects of Fiberglas on Animal and Human Skin, Indust. Med. **11**:482, 1942. Siebert, W. J.: Fiberglas Health Hazard Investigation, ibid. **11**:6, 1942. Hein, B. J.: Hazards of Exposure to Glass Wool, Glass Frit, or Foam Glass, J. A. M. A. **124**:187 (Jan. 15) 1944.

4. Scholz, R. P., and Mountjoy, P. S.: Fiberglas Suture Material, Am. J. Surg. **55**:619, 1942.

5. Maeth, H.: Fiberglas Used as a Root Canal Filling Material, Dent. Digest **51**:555, 1945.

6. Hirshfeld, J. W.; Williams, H. H.; Abbott, W. E.; Heller, C. G., and Pilling, M. A.: Significance of the Nitrogen Loss in the Exudate from Surface Burns, Surgery **15**:766, 1944.

addition, acrylic plates must be preformed and are not easily adapted to varying conditions encountered at the operating table.

Some form of wool has seemed logical, since it can be packed into the apex of the orbit and into inaccessible crevices, which are often present in fractures of the orbital floor. The introduction of "fiberglas" provided such a wool in suitable material.[7]

The operative procedure is essentially the same as that described previously for the subperiosteal implantation of cartilage in the floor of the orbit.[2] Instead of insertion of cartilage, however, a mass of "fiberglas" yarn is rolled into a ball, soaked in solution of penicillin for ease in handling and then packed firmly into the orbit until the eyeball has attained its proper level or until, in the anophthalmic socket, the upper lid has attained its normal full contour. The photographs show the preoperative and postoperative appearance of a patient in whom this procedure was carried out. This patient had traumatic enophthalmos with fracture of the orbital floor following a gunshot injury. The eye, amblyopic because of extensive traumatic chorioretinitis, was retracted 4 mm. and depressed a similar amount. A satisfactory cosmetic result was obtained after the insertion of glass wool. Similar results have also been obtained with patients who have had enucleations associated with loss of orbital volume.

It is believed that glass wool provides an inert, permanent and easily handled material for repairing defects which are primarily the result of deficiency in orbital content.

635 West One Hundred and Sixty-Fifth Street. (32).

7. "Fiberglas" is glass in the form of fiber or filament made by the Owens-Corning Fiberglas Corporation, Toledo, Ohio.

# BINASAL HEMIANOPSIA

JOSEPH IGERSHEIMER, M.D.
BOSTON

BINASAL hemianopsia is still a riddle in many respects and I can only present a critical report, including an interesting observation of my own, which in itself makes the problem still more difficult. A great deal has been published on binasal hemianopsia, but little is to be found in textbooks about this anomaly of the visual fields, probably because it is rarely encountered in individual practice.

I shall first present my own case.

## REPORT OF A CASE

A man aged 59, with chronic syphilis, came to the outpatient department of the Boston City Hospital for the first time on July 1, 1940, with the complaint that vision in his right eye had been gradually becoming worse in the past eight months and that reading with this eye was then very difficult. Vision was 3/200 in this eye and 20/70 in the left eye. Ophthalmoscopic examination revealed nothing abnormal. There was a slight contraction of the field in the nasal lower quadrant in the right eye and no contraction of the field in the left eye. Five weeks later the right eye did not show any change, whereas vision in the left eye was only 20/200, instead of 20/70. Again, five weeks later, on September 15, vision was found to be greatly deteriorated on both sides; it was limited to seeing fingers at a distance of 1 foot (30 cm.) in the right eye and of 5 feet (150 cm.) in the left eye.

The pupillary reaction in the right eye was sluggish. The disks were still of good color. There was binasal quadrantopsia, with a central scotoma in the right eye (fig. 1).

Except for the visual deficiency, the patient had few complaints—some headache, which was not severe, but no dizzy spells.

He was transferred to the neurologic service. The only neurologic abnormality noted was diminution to absence of the ankle jerk on the right side. The examiners also found independently a bilateral defect in the nasal quadrant of the visual field. A roentgenogram of the skull showed thinning of the floor of the sella turcica and of the posterior clinoid processes; there was an irregular area of calcification just above and anterior to the sella, probably in the walls of the internal carotid artery. In the pneumoencephalogram the shadow of the third ventricle appeared enlarged, but not displaced. The perichiasmal spaces were apparently not filled with air. There were no symptoms of involvement of the pituitary body.

---

Read before the New York Academy of Medicine, Section of Ophthalmology, March 18, 1946. A discussion of this paper was published in the October 1946 issue of the ARCHIVES, page 515.

On Oct. 18, 1940, an exploratory operation was performed by Dr. Donald Munro. The dura was pulsating and not particularly tense. On elevation of the right frontal lobe it was apparent that a tumor of some sort lay in relation to the right optic nerve, which was superomedial to the mass. The tumor was pulsating and was about the size of an English walnut. It had the appearance of an aneurysm, and consequently no attempt was made to expose it in detail. The wall was punctured with a fine hypodermic needle, and arterial blood was withdrawn into a syringe. The puncture hole did not bleed. The wound was closed.

Recovery was good, and three weeks later, just before the patient was discharged, another determination of the field revealed total nasal hemianopsia, instead of a quadrantopsia, in the left eye and vision in the right eye was limited to perception of hand movements in the upper part of the temporal field.

About four months later (March 21, 1941) the patient returned to the outpatient department of the ophthalmic service. He was in good health and spirits. In the

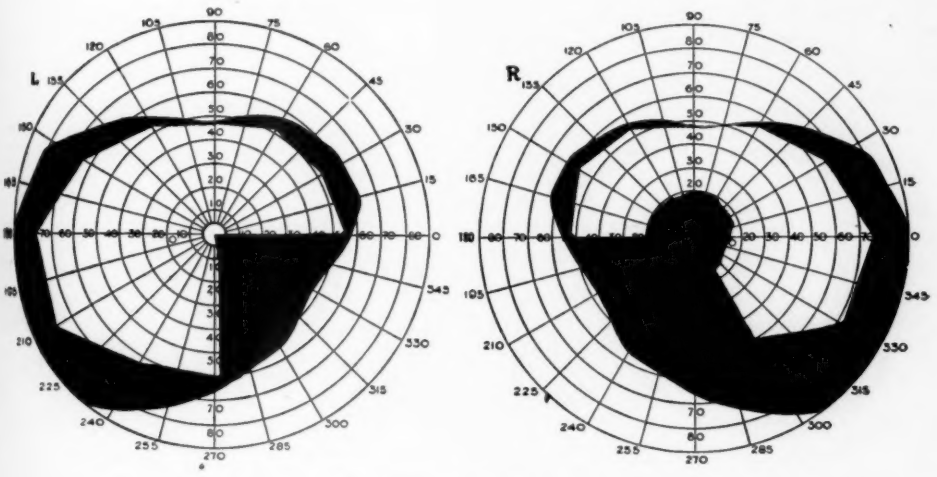



Fig. 1.—Visual fields at time of first examination, showing binasal quatranopsia with central scotoma in right eye.

right eye only a small portion of the visual field remained and the disk was pale, but in the left eye vision was improved from counting fingers to 20/50; there was still some contraction of the lower nasal part of the field. Some time later vision in this eye became 20/20 again, and the field showed no residual defect. The disk was of normal color (fig. 2).

Such was the visual status up to the time of writing. The patient, meanwhile, had had several attacks of unconsciousness and convulsions, which were considered post-traumatic epilepsy. A roentgenogram in September 1945 showed curvilinear areas of calcification slightly to the right of the midline and anterior to the pituitary gland. This area of calcification measured about 2 cm. by 8 mm. and was probably due to an aneurysm of the circle of Willis. The floor of the sella was depressed and thinned. The posterior clinoid processes showed slight thinning.

*Summary.*—An aneurysm lay in relation to the right optic nerve, being lateral to and apparently covered by the nerve. How far back this

aneurysm reached could not be determined. Binasal quadrantopsia was also present, combined on the right side with a central scotoma. In the left eye the macular fibers must also have been involved to a certain degree, as vision had deteriorated to such an extent. At the exploratory operation the tumor was not touched except for withdrawal of a very small amount of blood. Nevertheless, vision in the left eye regained its full strength. Interesting, in the first weeks after the operation total nasal hemianopsia developed in the left eye; then the defect of the visual field disappeared altogether. On the left side the optic disk had always a normal color, whereas on the right side the degeneration was progressive.

From the patient's history, it is probable that the visual disturbance started with a central scotoma on the right side. The nasal defect

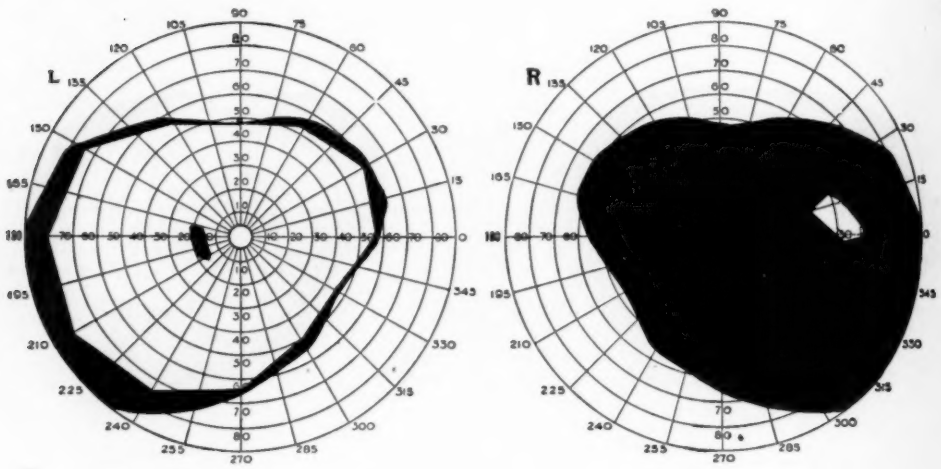



Fig. 2.—Visual fields after operation, showing recovery of vision in left eye.

was first found in the right eye and later also in the left eye. It seems to be not unusual that bitemporal, as well as binasal, hemianoptic defects are first noted in one eye (Holmes,[1] Baudouin, Halbron and Deparis[2]).

The aneurysm in my case belongs to the supraclinoid type of saccular aneurysms, which have no relation to the cavernous sinus and are therefore not complicated by ocular palsies or involvement of the fifth cranial nerve (Jefferson[3]). Although the patient had long-standing syphilis, it is doubtful whether the aneurysm had any relation to the syphilitic infection, as most aneurysms of the circle of Willis

1. Holmes, G.: Tr. Internat. Ophth. Cong. **5**:65, 1929.
2. Baudouin, A.; Halbron, P., and Deparis, M.: Rev. neurol. **2**:531, 1934.
3. Jefferson, G.: Brain **60**:444, 1937.

are found in nonsyphilitic persons (Fearnsides,[4] Jefferson,[3] Ayer[5]). Supraclinoid aneurysms comprise those of the anterior cerebral and the anterior communicating artery.

It seems characteristic of this kind of aneurysm for the visual fields to vary or fluctuate. In my case there was a steady progression for the worse, but the patient was not often enough confronted with tests of visual function to permit confirmation or denial of such a variation.

Unilateral amaurosis (or amblyopia) and bitemporal hemianopsia seem to be the favorite visual defects associated with supraclinoid aneurysms, as well as with aneurysms of the internal carotid artery. Homonymous hemianopsia occurs occasionally (e. g., Dott,[6] case 6). Of 12 cases reported by Walsh and King,[7] with aneurysms of the internal carotid artery or the anterior branch, there was bitemporal hemianopsia in 1, paracentral scotoma on one side in 1 and apparently normal visual fields in 6; in 4 cases the fields were not determined. Jefferson [3] stated that involvement of the inferior fields in the early stages is in favor of the diagnosis of aneurysm rather than of tumor of the pituitary.

In the whole literature I could find only 3 cases of binasal hemianopsia. Two of them (Hornicker,[8] Noiszewski [9]) were reported only briefly, without charts of the visual fields. In Hornicker's case the diagnosis was made roentgenographically; in Noiszewski's, on the basis of a bruit. In a third case, in Olivecrona's service, reported by Sjöqvist,[10] the diagnosis was also made by roentgenographic methods. As in my case, binasal quadrantopsia was found, a clinical observation difficult to bring in line with an aneurysm of the internal carotid artery. My case seems to be the first instance of binasal hemianopsia in which the lesion was verified by autopsy. As in other cases of saccular aneurysm, arteriosclerosis was present and was evident in the roentgenograms as calcification.

There now arises the main question—how to explain binasal hemianopsia in general, and a case like mine in particular. Can binasal hemianopsia be used as a localizing sign, as one is accustomed to do in bitemporal defects?

In discussing the various sides of the question, it might be well to follow the course of the nerve fibers on their way from the optic nerve to the optic tract.

---

4. Fearnsides, E. G.: Brain **39**:225, 1916.

5. Ayer, J. B.: New England J. Med. **228**:423, 1943.

6. Dott, N.: Edinburgh M. J. **40**:219, 1933.

7. Walsh, F. B., and King, A. B.: Ocular Signs of Intracranial Saccular Aneurysms, Arch. Ophth. **27**:1 (Jan.) 1942.

8. Hornicker, E.: Klin. Monatsbl. f. Augenh. **72**:766, 1924.

9. Noiszewski, K.: Klin. Monatsbl. f. Augenh. **39**:402, 1901.

10. Sjöqvist, O.: Nervenarzt **9**:233, 1936.

In many textbooks the discussion of the course of the nerve fiber-bundles in the peripheral visual pathways is oversimplified and makes it appear that the uncrossed fibers have always a temporal location from the optic nerve to the external geniculate body and the crossed bundles always a medial location.

Dejerine [11] stated that although there exist crossed and uncrossed bundles in the intracranial portion of the optic nerve the corresponding fibers are not totally separated, but are partly intermingled. But he did not deny Henschen's [12] opinion that the uncrossed bundles are mainly in the lower temporal part of the intracranial portion of the optic nerve. This intermingling is still more pronounced in the chiasm.

In studying Wilbrand's [13] classic description, one finds not only that the fibers in the nasal part of the optic nerve are displaced medially by the strong pial septum in the dorsal aspect, but that a large part of the temporal fibers are turned at right angles and belong to the crossed bundles. This pial spur is microscopically the starting point of the chiasm. Most of the fibers which are going to cross in the chiasm to the other side are gathered together in the dorsomedial part of the end of the intracranial portion of the optic nerve. The fibers which are not to cross are located mainly in the lower temporal part of the intracranial portion of the nerve and seem to be separated particularly in the short distance (several millimeters) between the pial spur and the anatomic chiasm.

A large number of the nasal fibers, before they enter the chiasmal body, run through the anterior commissure to the fellow optic nerve in a downward direction and form there in the lower part the "knee." Only after this detour do they spread into the chiasm, and one can find them in the temporal part of that structure, as well as in the more medial part; but the number of the fibers is greater in the ventral layers of the chiasm than in the dorsal layers. There are also crossed fibers coming, for example, from the right optic nerve which runs toward the right optic tract, form there the so-called posterior knee and run then through the posterior commissure into the left optic tract.

Wilbrand differentiated a third group of crossed fibers, which were characterized by a more horizontal course from one lateral angle of the chiasm to the other. Wilbrand came to the same conclusion as Dejerine, namely, that everywhere in their course through the chiasm the uncrossed fibers are surrounded by crossed fibers, that they are located mainly in the temporal part of the chiasm, but that they in

11. Dejerine, J.: Anatomie des centres nerveaux, Paris, J. Rueff, 1901, vol. 2.

12. Henschen, S. E.: Klinische und anatomische Beiträge zur Pathologie des Gehirns, Upsala, Almquist & Wiksell, 1890-1892.

13. Wilbrand, H.: Ztschr. f. Augenh. **59**:135, 1926. Wilbrand, H., and Saenger, A.: Neurologie des Auges, Wiesbaden, J. F. Bergmann, 1904, vol. 3, p. 1.

part spread toward the central part without reaching the midline, and that they join in the dorsolateral part of the optic tract. According to Hartmann and David,[14] it is probable, but not proved, that the uncrossed fibers which spread toward the center of the chiasm come from the upper temporal quadrant of the retina. The center of the chiasm is mainly occupied by the macular fibers.

Considering these microscopic observations, it is hard to believe that pressure from sclerosed arteries or from a syphilitic exudate in the meninges on both lateral angles of the chiasm can produce a clearcut binasal hemianopsia. Also, clinical proof for such an occurrence is lacking. Only in a case reported by Behr,[15] in which both sides of the chiasm showed indentation by a sclerosed artery and in which the defect in the visual fields was mainly binasal was an anatomic degeneration present, increasing toward each angle. But even this case is not fully convincing. In the event, of course, that, in addition to the binasal defect, the temporal fields become defective, there is up to a certain degree no theoretic objection to the assumption of pressure from both sides as a cause of binasal hemianopsia, but often the visual field will not then be characteristic.

That the pressure on the chiasm from below causes bitemporal, and often irregular, field defects is common clinical knowledge. Only in the advanced stages of tumor of the pituitary gland do the lower nasal quadrants of the fields become involved. Binasal hemianopsia associated with enlargement of the pituitary gland, if it really occurs at all, is rare indeed.

How is it, now, with pressure from above as a cause of binasal hemianopsia?

It is true that in many cases of more or less typical binasal hemianopsia in which autopsy was performed a cerebral tumor was observed at a distance from the chiasm, but in a subtentorial location. Cushing and Walker[16] encountered this type of hemianopsia in 5 to 6 per cent of their 300 cases of cerebral tumor. They explained the visual defect as due to secondary hydrocephalus and distention of the third ventricle. The enlarged third ventricle lies on the dorsal aspect of the chiasm and may even extend to both angles of the chiasm. Bing (cited by Lutz[17]), Traquair and associates[18] and others really assumed that degeneration of the chiasmal fibers would be the result of such pressure. Such a

14. Hartmann, E., and David, M.: Les affections due chiasma, in Bailliart, P.; Coutela, C.; Redslob, E., and Velter, E.: Traité de'ophtalmologie, Paris, Masson & Cie, 1939, vol. 6, p. 877.

15. Behr, C.: Arch. f. Ophth. **75**:210, 1910.

16. Cushing, H., and Walker, C. B.: Arch. Ophth. **41**:559, 1912.

17. Lutz, A.: Arch. f. Ophth. **119**:423, 1928.

18. Traquair, H. M.; Dott, N. M., and Ritchie, R. W.: Brain **58**:398, 1935.

possibility cannot be denied, but there seem to be no cases in the literature to prove it. On the contrary, there is no doubt that the third ventricle can be greatly distended without any consequences to the chiasm. I have slides in my collection from a case of cerebral tumor with papilledema and enormous dilatation of the third ventricle. Vision and the visual fields were normal, and microscopic examination of the optic nerves and the chiasm in sections stained by the Weigert method did not show any degeneration. But assuming that pressure from a dilated third ventricle or a tumor in this ventricle does exert an effect on the chiasm, could this pressure be the cause of binasal hemianopsia? The basis for such an assumption must be that the uncrossed fibers are united in some part of the chiasm and can be damaged there as a unit. There was a time, long ago, when such an assumption seemed justified, for Bernheimer,[19] in his studies on myelination, observed that the dorsal part of the chiasm contained uncrossed fibers only. But neither Dejerine nor Wilbrand could confirm Bernheimer's results, and the idea of explaining binasal hemianopsia on the basis of a single focus in the dorsal area of the chiasm had to be abandoned. It is true, however, that in the posterior portion of the chiasm the uncrossed fibers are chiefly in the dorsal layers of the chiasm and the crossed fibers chiefly in the ventral layers, but there is nowhere an actual separate fascicle.

Thus, it is evident that binasal hemianopsia occurring in a case of cerebral tumor cannot be explained by pressure in the chiasm from secondary hydrocephalus. According to Cushing and Walker, distention of the third ventricle pushes the optic nerves downward and outward against the carotid arteries, transversely indenting the outer aspects of the nerves.

But there is another explanation which must be considered. Cushing and Walker stated that in all their cases with binasal hemianopsia there was papilledema and that this papilledema was in a rather advanced stage. In a series of cases reported by Vincent and Hartmann [20] showing binasal hemianopsia there was also papilledema, and in some of their observations no tumor but optochiasmatic arachnoiditis was present; in their first case it is even noted that the ventricles were very small.

Central vision was decreased in most of their cases, proving that the process in the optic nerve was not in an early stage; and besides the nasal hemianopsia there was a defect in the temporal field. Therefore, it seems most plausible to explain the binasal defect not by pressure itself but by the degenerative process in the optic nerves. It is well known that in such cases of secondary atrophy following papilledema

19. Bernheimer, L., in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde ed. 2, Leipzig, W. Engelmann, vol. 1, chap. 6, p. 10.

20. Vincent, C., and Hartmann, E.: Ann. d'ocul. **171**:193, 1934.

there is no regularity in the amount of degeneration. Why should not once in a while, as an accident, the uncrossed fibers in both nerves degenerate first? This explanation of accidental involvement holds true in cases of tabetic atrophy of the optic nerve with binasal hemianoptic fields. I published a case of rapid visual decrease in a man with rapidly progressive hypertensive vascular disease. Although there was microscopically widespread degeneration of the optic nerve, tests of the fields showed that the uncrossed fibers were especially involved. This case is sometimes mentioned in the literature as an instance of binasal hemianopsia; I never thought of it in this way. No one would speak of binasal hemianopsia in a case of advanced glaucoma in which only the temporal fields were still functioning.

Such a simple explanation of accidental involvement of the uncrossed fibers is, of course, not valid for cases of hemianopsia with a sharp midline and is not plausible for cases of papilledema in which the central vision is still normal.

From the foregoing discussion, I conclude that binasal hemianopsia cannot be produced by a lesion within the chiasm, or probably by a pathologic process surrounding the chiasm. This conclusion, of course, does not apply to the intracranial portion of the optic nerves, especially the part just in front of the chiasm, between the pial septum and the chiasm. Here the temporal bundles are fairly well isolated, and there is no objection to the assumption that pressure on both sides could cause a binasal field defect. In these circumstances, one can understand that binasal quadrantopsias and hemiachromatopsia (Lutz,[17] Seguini [21]) may occur, but never binasal hemianoptic scotomas. The classic case of pressure on the peripheral pathways producing binasal hemianopsia is that of Herman Knapp.[22] The internal carotid and the anterior cerebral arteries were placed astride the chiasm, being in immediate contact with its outer sides and those of the optic nerves. The pressure on the optic nerve seems to be the more important factor in producing the field defect. The chiasm and the optic nerves appeared unusually flattened and atrophic. It is interesting, but not easy to understand, that in this case the visual field of one eye became normal during the course of the disease.

Other authors, such as Lutz,[17] Loewenstein,[23] Hartmann and David[14] and others, similarly concluded that binasal hemianopsia can be explained only by pressure of the intracranial portion of the optic nerves against some hard tissue, probably most frequently sclerosed arteries. It is only

21. Seguini, A.: Riv. oto-neuro-oftal. **4**:299, 1927; abstracted. Zentralbl. f. d. ges. Ophth. **19**:144, 1928.

22. Knapp, H.: Arch. Sc. & Pract. Med. **1**:304, 1873.

23. Loewenstein, A.: Med. Klin. **31**:176, 1935.

strange that, although advanced sclerosis of the circle of Willis is relatively often to be noted, binasal hemianopsia is a rare event.

This discrepancy is perhaps due to the different way in which the optic nerves react to pressure from outside. It has been seen that even extreme dilatation of the third ventricle may leave no marks on the chiasm. I wish also to mention the older illustrations, in which one can see the intracanalicular portion of the optic nerve so greatly compressed by the sclerotic ophthalmic artery that a deep indentation is produced, or the nerve even is split into two parts. Nevertheless, in several cases of this type no degeneration was demonstrable anatomically. The slower and more chronic the action of such a pressure, the less, apparently, is the damage. But I wish by no means to imply that such a pressure is always harmless. The Foster Kennedy syndrome is a well known sign of a pressure effect. This syndrome, or a part of it, the central scotoma, can be produced not only by a meningioma, but occasionally also by an aneurysm (Kennedy [24]), optochiasmatic arachnoiditis (Yaskin and Alpers [25]) or sclerosis of the internal carotid arteries (Yaskin and Schlezinger [26]). An observation of Schloffer,[27] seems to be especially interesting in this, and in another, respect. A patient aged 65 was operated on for meningioma. He had extremely reduced vision in both eyes—a central scotoma and atrophy of the optic nerve in the right eye and papilledema and constriction of the nasal field in the left eye. There was also definite hyposmia. Operation and postmortem examination revealed no tumor, but the optic nerves were flattened and distorted by sclerotic arteries. Microscopic study showed that almost the whole cross section of the right optic nerve was degenerated, although the outer visual field was good; damage to the left optic nerve was much less, but here also, there was degeneration.

It is noteworthy that in this well studied case there was no harmony between the clinical and the anatomic observations so far as the visual field was concerned. Baurmann,[28] in a case of cerebral tumor with binasal hemianopsia, made a reconstruction model of the optic nerves and chiasm and found that there was no parallelism between the microscopic lesions in the nerves and the indentations produced by the sclerosed arteries.

---

24. Kennedy, cited by Meves.

25. Yaskin, H. E., and Alpers, B. J.: Foster Kennedy Syndrome with Post-Traumatic Arachnoiditis of Optic Chiasm and Base of Frontal Lobes, **34**:399 (Nov.-Dec.) 1945.

26. Yaskin, H. E., and Schlezinger, N. L.: Foster Kennedy Syndrome Associated with Non-Neoplastic Intracranial Conditions, Arch. Ophth. **28**:704 (Oct.) 1942.

27. Schloffer, H.: Med. Klin. **30**:421, 1934.

28. Baurmann, M.: Arch. f. Ophth. **126**:203, 1931.

I conclude from these, and from other, experiences that the effect of pressure on the optic nerves differs from that of pressure on the chiasm and that in a number of cases the fibers in the neighborhood of the pressure agent are not, or are not mainly, affected. This, perhaps, explains why one so seldom sees binasal hemianopsia, although cases in which sclerotic arteries press on the peripheral optic pathways are rather frequent.

All explanations have a bearing on the question of how to explain a binasal hemianopsia in a case like mine, in which an aneurysm pressed on one optic nerve only.

One more point must be considered. This is the blood supply of the chiasm and the intracranial portion of the optic nerves. Little is known about the details of this blood supply and still less about the pathologic processes involved. These questions offer a worthwhile field of research. I was engaged in such studies, but I had no opportunity to continue them. Traquair, Dott and Russell [18] mentioned an interesting observation. A suprasellar tumor in a woman with bitemporal hemianopsia was successfully removed. The patient had also arteriosclerosis. Vision was good after the operation, but a short time later she became blind. Postmortem examination showed necrosis of the chiasm and the optic nerves, apparently caused by thrombosis of the small arteries. How often such or slighter nutritional disturbances occur is not known. But it may be that this factor, in addition to the mechanical one, has a certain significance.

The present case is one in which an explanation of the visual defect is especially difficult. The aneurysm lay beneath the right optic nerve and on its temporal side, and after a central scotoma and a nasal field defect had appeared in the right eye the nasal defect developed in the left eye. The effect on the left eye was only temporary and disappeared entirely some time after the exploratory operation. A similar confusing case was published by Cushing [29] (case 10), as well as cases by Jefferson (cases 7 and 8) and perhaps by others. Cushing observed an aneurysm beneath the intracranial portion of the right optic nerve and the right side of the chiasm. The situation would have led one to suppose that the field defects in the right eye had started with a nasal hemianopsia, stated Cushing,[29] but the visual trouble really started with left temporal hemianopsia. In his case, as in mine, the visual function improved greatly after operation; however, if the process has been going on too long total amaurosis may result in both eyes, even though the aneurysm is strictly one sided, as in cases described by Ogle [30] and by Roe.[31]

29. Cushing, H.: Tr. Internat. Ophth. Cong. **3**:156, 1929.
30. Ogle: Brit. & For. Med.-Chir. Rev. **36**:494, 1865.
31. Roe, H.: Proc. Path. Soc., London **3**:46, 1850.

## CONCLUSION

I conclude with some certainty that the field of action in a case of binasal hemianopsia is not the chiasm but the short portion of the intracranial part of the optic nerve in front of the chiasm. If the lesion is unilateral and the other optic nerve is also involved, this involvement can be explained only mechanically by pressure against the nerve, probably of sclerosed vessels, or by a local nutritional deficiency. Such a nutritional pathogenesis seems more likely, for an exploratory operation would hardly change the nature of a hard artery pressing on the nerve, and could not explain improvement such as was seen in my case and in others. I believe, with Caramazza,[32] that the presence of binasal hemianopsia combined with unilateral central scotoma is in favor of a vascular disease in the middle fossa and against the possibility of a tumor of the pituitary body or of a suprasellar tumor.

483 Beacon Street.

32. Caramazza: Riv. oto-neuro-oftal. **50**:9, 1932; cited by Schloffer.[27]

# Clinical Notes

## A MODIFIED FORCEPS FOR INTRACAPSULAR EXTRACTION OF CATARACT

DAVID KADESKY, M.D., SAN FRANCISCO

This capsule forceps is peculiar in the construction of the grasping jaws; that part of the blades which grasps the capsule is concave and shaped to meet a convex curve with a radius of 10 mm., thus approximating the average convexity of the anterior surface of the lens. On their under surface the blades meet each other exactly throughout their length. Their distal ends are slightly rounded, so that there are no sharp edges or points. The cross section of the blade is triangular, with the base downward, allowing any excess of capsule to well up between the blades without obstruction. Pressure is controlled by a stop, so that

Fig. 1.—Straight action forceps.

Fig. 2.—Details of the jaw.

the capsule is not crushed. The instrument is made in both a straight action and a cross action model, the latter permitting the surgeon to relax his wrist and fingers while manipulating the lens. There is a tendency, however, to press on the blades of the forceps, thereby opening the jaws and thus breaking the hold on the capsule. This would naturally occur if one were unaccustomed to cross action forceps. For this reason many prefer the uncrossed model.

The forceps has been used in more than 300 cataract extractions and has succeeded in subluxating the cataract in 82 per cent of the cases; in the remaining 18 per cent the capsule tore.

The instrument was made by Mr. E. A. Black, of V. Mueller & Co., Chicago.

408 S. Honore.

From Green's Eye Hospital.

## USE OF ONE CONTACT LENS IN CORRECTION OF HIGH UNILATERAL MYOPIA

CHARLES LITTWIN, M.D., NEW YORK

Mr. R. D. L., aged 30, an engineer, came to me for help, complaining of vision with his present spectacles.

For the past nine years he had been wearing glasses. One of 3 children, he was the only sibling with defective eyesight. His mother had a high amount of myopia in the right eye, and her left eye was emmetropic. His brother and

sister both had normal vision. His condition was identical with that of his mother. His error of refraction was as follows: Right eye, —13.00 D sph., visual acuity 20/50—; left eye: —0.25 D. cyl., axis 180, vision 20/20.

The high amount of myopia in the right eye corrected gave him a size-image difference. In August 1945 he was measured for his aniseikonia, and iseikonic lenses were prescribed. These spectacles gave him fusion and comfort, but only when the eyes were in primary fixation. As he moved his eyes in the normal ocular excursions, the "image" of the right eye appeared "barrel shaped," and diplopia was manifested. It was this condition that brought him to me for relief.

In fitting the patient with a contact lens for the right eye, I made objective studies with test lenses,[1] and found that the horizontal and vertical curves of the sclera were 14.0 by 13.4 mm., respectively. Although the sclera was toroidal, there was no astigmatism, either subjectively or with the retinoscope. In tests for corneal clearance, a 9.0 mm. radius gave about 1.5 mm. clearance, and a —10.00 D. correction incorporated in the contact lens gave vision of 20/50+. The duochrome test showed the eye to be emmetropic, but with a +1.00 D. lens in a spectacle lens over the right eye vision was improved to 20/30+, and the —0.25 D cylinder over the left eye gave 20/20 vision. (The +1.00 D correction incorporated in the finished contact lens changed his visual acuity with the duochrome test as well as with the Snellen letters.)

Although the +1.00 D. correction in the glass over the right eye while he wore a contact lens correcting his myopia really made an optical system like a Galilean telescope, it was not the size-image difference that corrected his diplopia and gave him comfort; it was the ability of the eyes to move in their natural ocular excursions without suffering the prismatic effect (since the lens moved with the eye) which gave him fusion in the eight cardinal positions.

The patient was urged to be measured again for aniseikonia, but, with the comfort he then received, he was satisfied with the contact lens and the spectacles. Without the spectacles, his vision is 20/50+, and he still has fusion in all cardinal points. He uses the contact lens while swimming and experiences no asthenopia for six to eight hours without changing.

Indeed, the use of one contact lens has made a changed man of my patient for the better.

550 Park Avenue.

1. The Master Test Set, made by the National Contact Lens Corporation, of New York.

# News and Notes

EDITED BY DR. W. L. BENEDICT

## GENERAL NEWS

**The Dartmouth Eye Institute Passes.**—June 30, 1947 marked the passing of the Dartmouth Eye Institute. The research man, Dr. Kenneth Ogle, has joined the Mayo Clinic; the ophthalmologist, Dr. Hanford L. Auten, has joined the Hitchcock Clinic; the optometrists have gone into private practice. Mr. A. Ames Jr. and Mr. John Pearson, who has been director of the Dartmouth Eye Institute since the death of Dr. Bielschowsky, have formed the Hanover Institute.

**International Ophthalmic Council.**—At the recent meeting of the International Ophthalmic Council, held in Paris, May 18, 1947, it was decided to hold the next meeting in London in 1950, the president to be Sir Stewart Duke-Elder and the vice president, Dr. P. Bailliart. Plans for symposiums on the following subjects were adopted: (1) "The Vegetative Nervous System and Its Disorders in Relation to the Eye"; (2) "Hereditary Diseases in Ophthalmology."

**American Board of Ophthalmology.**—At the last meeting of the American Board of Ophthalmology, it was decided to replace the personal preliminary interview with a written qualifying test for all applicants. This is, in part, to save them the expense and time in traveling long distances to cities where national meetings are held. The written tests, therefore, were given simultaneously in many parts of the country on Wednesday, July 23, 1947, at 1:00 p. m., and will be given again during the winter, 1947-1948. Candidates then qualifying will be admitted to the practical examination.

Registration for Chicago, Oct. 7-12, 1947, has been closed and is limited to 60 candidates.

## UNIVERSITY NEWS

**Dr. Glen G. Gibson Succeeds the Late Dr. Walter I. Lillie.**—Dr. Glen G. Gibson, who was associate professor of ophthalmology of Temple University Medical School and Hospital, has been advanced to the rank of professor and head of the department of ophthalmology.

Dr. Gibson studied at the Gonzaga University and graduated from the St. Louis University School of Medicine in the class of 1930. His internship was served at Providence Hospital, Detroit, after which he took a postgraduate fellowship in ophthalmology at the Mayo Clinic. After finishing his training at the Mayo Clinic, he came to Temple University as an assistant to Dr. Lillie and remained associated with him for ten years.

Dr. Gibson is a member of the American Ophthalmological Society, the American Medical Association, the American Academy of Ophthalmology and Otolaryngology and the College of Physicians of Philadelphia. His contributions to scientific journals have been numerous.

## SOCIETY NEWS

**Irish Ophthalmological Society.**—The Irish Ophthalmological Society held a general meeting at the Royal Victoria Eye and Ear Hospital in Dublin, on May 22 and 23, 1947, with Dr. H. B. Goulding in the chair. The following papers were submitted on the first day: "Military Ophthalmology: the Mobile Ophthalmic Unit," Dr. D. H. Douglas; "Responsibilities of Ophthalmology to Industry," Dr. A. J. Mooney; "Orbital Metastases from Wilms's Tumor," Dr. H. B. Goulding. The Montgomery Lecture was given by Prof. Bernard Samuels, of New York, on "Problem of Sympathetic Ophthalmia." A visit was made to the Hospital Orthoptic Clinic, and cases were demonstrated in the hospital. On the second day the following papers were presented: "Proptosis: Report of Cases," Dr. J. B. McArevey; "Blindness Following Sympathetic Ophthalmia of Six Years' Standing: Operation; Recovery," and "Tumor in the Orbit of a Child, Possibly Secondary and Suggestive of That Described by Hutchinson," Dr. W. A. Anderson; "Roentgenograms of Gross Intracranial Foreign Bodies (Battle Casualties)," Dr. L. B. Somerville-Large; "Bone Formation in the Uvea," Prof. Bernard Samuels.

**Chicago Ophthalmological Society.**—The Chicago Ophthalmological Society will give a forty hour refresher course December 8 to 13, inclusive. The faculty will include members of the departments of ophthalmology of the University of Chicago, the University of Illinois, Loyola University and Northwestern University and staff members of all the principal hospitals of Chicago. Instruction will consist of didactic and practical courses, emphasis being placed on the practical courses given to small groups. Physicians practicing ophthalmology or ophthalmology, otology, rhinology and laryngology are eligible for the course. The fee will be $100. For details, write to the registrar, Miss Maude Fairbairn, 8 West Oak Street, Chicago.

**North Carolina Eye, Ear, Nose and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology.**—The second annual meeting of the North Carolina Eye, Ear, Nose and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology will be held at the Hotel Skyland, in Hendersonville, N. C., on Sept. 15, 16, 17 and 18. The first two days will be devoted to ophthalmology, and the guest speakers will be Dr. Harold Brown, Dr. John H. Dunnington, Dr. Jack Guyton and Dr. Brittain F. Payne.

**American Ophthalmological Society.**—At the recent annual meeting of the American Ophthalmological Society the following officers were elected for the coming year: president, Dr. Henry C. Haden; vice president, Dr. Bernard Samuels; editor, Dr. Wilfred E. Fry; secretary-treasurer, Dr. Walter S. Atkinson.

## PERSONAL NEWS

**Dr. Alfred E. Maumenee Succeeds Dr. Hans Barkan, Who Becomes Professor Emeritus of Ophthalmology, Stanford University School of Medicine.**—Dr. Hans Barkan, now clinical professor of ophthalmology and chief of the division of Ophthalmology at Stanford University School of Medicine, becomes emeritus professor on Sept. 1, 1947.

Dr. Alfred E. Maumenee, now at Wilmer Ophthalmological Institute, in Baltimore, has been appointed professor of surgery assigned to ophthalmology, to succeed Dr. Barkan. Dr. Maumenee will not assume his duties at Stanford University until Sept. 1, 1948. In the meantime, Dr. Dohrmann Kaspar Pischel, clinical professor of ophthalmology at Stanford, will act as chief of the division until Dr. Maumenee can join the staff.

**Appointment of Dr. William H. Buschke.**—Dr. William H. Buschke has been appointed research ophthalmologist to the Manhattan Eye, Ear and Throat Hospital, New York, and will be in charge of the Ayer Foundation Ophthalmic Research Laboratory at this hospital. The aims of the Ayer Foundation and of its research project, which was initiated by Dr. R. Townley Paton, are directed toward problems of the general physiology and experimental pathology of ocular tissues, with primary, but not exclusive, emphasis on the cornea. The Ayer Laboratory is being installed jointly by the Foundation and by the hospital. It is not a part of the Eye Bank for Sight Restoration, Inc., which is located at the same hospital and the research activities of which tend more toward applied problems.

Dr. Buschke, who is a graduate of the University of Berlin, received his ophthalmologic training at the university ophthalmic hospitals in Berlin and in Basel and Bern, Switzerland, and has since 1938 been associated with the Wilmer Ophthalmological Institute of Johns Hopkins University and Hospital, first as research fellow and later as instructor in ophthalmology. He is a member of the American Medical Association, the American Physiological Society, the New York Academy of Sciences and the Swiss Ophthalmological Society. The principal subjects of his previous work are: role of vitamins in ophthalmology, physiologic factors controlling light sense, experimental and classification studies on cataracts, studies on the mechanism of secretion in the ciliary body and on the physiology of epinephrine and experimental studies on the general physiology and pathology of the corneal epithelium (mitosis, nuclear pathology, wound healing). Several of these studies have been carried on during his research association for the past nine years, and in cooperation with Dr. Jonas S. Friedenwald.

## Correspondence

### THE MODIFIED LIÉGARD CORNEOSCLERAL SUTURE

*To the Editor*:—The original description of the technic for a modified Liégard corneoscleral suture in cataract surgery which Dr. Otis S. Lee Jr., of Iowa City, reports in the Archives of May 1947, was made by Dr. E. H. Frisch, of Atlantic City, N. J. (A method for Preventing Loss of Vitreous, *Am. J. Ophth.* **5:** 81 Feb. 1922). This was brought forward by Dr. William Zentmayer in a comment when an almost similar suture was described before the Section on Ophthalmology of the College of Physicians of Philadelphia on April 20, 1944 (Arch. Ophth. **32:** 522 Dec. 1944).

Carroll R. Mullen, M.D., Philadelphia.

2025 Locust Street.

# Obituaries

## EDWARD COLEMAN ELLETT, M.D.

**1869-1947**

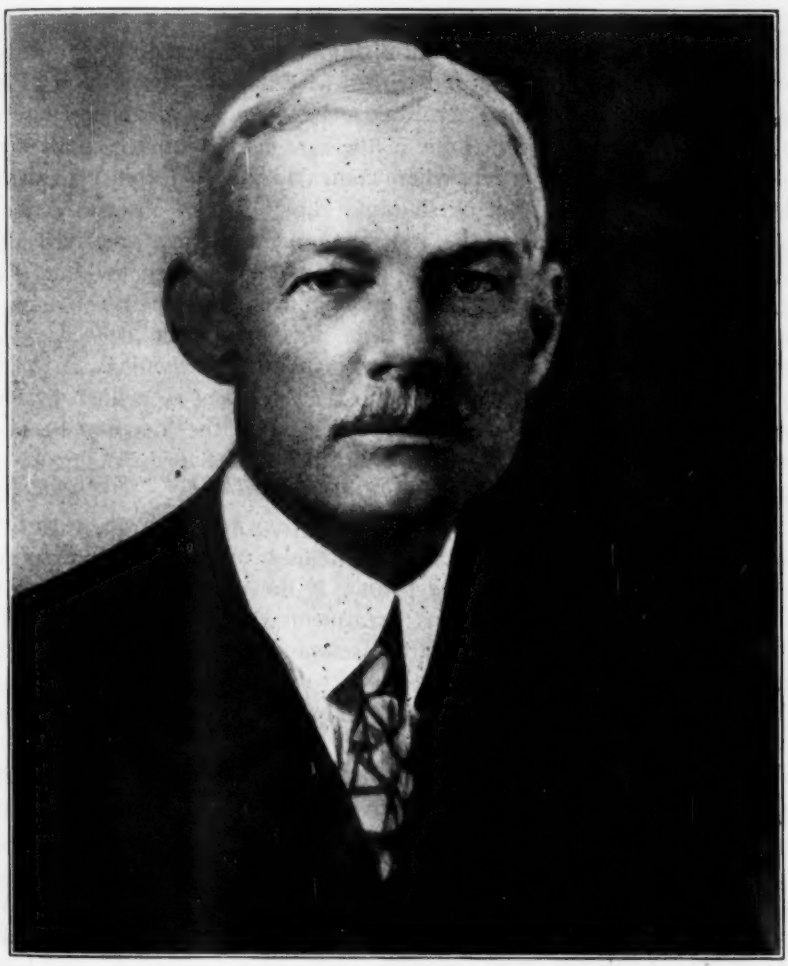
Dr. Edward Coleman Ellett, internationally famous for his contributions to ophthalmology, died in Atlantic City Hospital, June 8, 1947, after an attack of coronary thrombosis, suffered on the train while en route to the centennial celebration of the American Medical Association. During the previous week, at the meeting of the American Ophthalmological Society in Hot Springs, Va., he had participated freely in the discussions and seemed as usual, although he and his close friends were aware that such an attack was imminent. His practice for the past eighteen months had been restricted to consultation and surgery, but his interest in the specialty was in no wise diminished.

Dr. Ellett, son of Judge Henry T. and Katherine Coleman Ellett, was born in Memphis, Tenn., Dec. 18, 1869. He was educated in private schools in Memphis, attended for two years the Southwestern Presbyterian University at Clarksville, Tenn. (now Southwestern College, at Memphis) and received his degree of Bachelor of Arts from the University of the South, Sewanee, Tenn., in 1888. These two institutions later conferred on him the honorary degrees of LL.D. and D.Sc.—the former by Southwestern College, in 1942; the latter by the University in Sewanee in 1943. His medical degree was received at the University of Pennsylvania in 1891, where he was also honored with the Alumni Medal for the highest scholastic average in his class. After a year as resident physician in St. Agnes Hospital, Philadelphia, and a year as house surgeon at Wills Hospital, he returned to Memphis, in 1893, where he confined his practice to diseases of the eye, ear, nose and throat, and since 1917 to diseases of the eye only.

In 1896 he married Nina Polk Martin, and their union endured for over a half-century, a fine example of mutual devotion. She was the perfect complement to his professional life, smoothing out the home affairs so as to give him a maximum of time for writing and organizing his medical material. Their interest in travel was gratified by many trips abroad and to South and Central America, where the work of various surgeons was observed and lasting friendships were formed. She was with him in Hot Springs and Atlantic City. They had no children.

Dr. Ellett was professor of Ophthalmology in the medical department of the University of Tennessee from 1906 to 1922, and chief of staff of the Memphis Eye, Ear, Nose and Throat Hospital from its opening, in 1926,

until his death. His main interest was in graduate teaching, and from the organization of the instructional courses of the American Academy of Ophthalmology and Otolaryngology to the present, he annually gave an hour of instruction on some subject of clinical interest. Any intern, resident or visitor who manifested the least interest in what "The Colonel" was doing was cordially invited to the operating room and was



EDWARD COLEMAN ELLETT, M.D.
1869-1947

welcomed at ward rounds. He was the motivating influence behind annual "clinic days" which for years the Memphis Society of Ophthalmology and Otolaryngology held for the interested specialists of the Mid-South area.

Dr. Ellett's contributions to the literature of ophthalmology are too numerous to record. His interest was mainly in clinical ophthalmology, and his reports dealt with his long personal experience with various phases of the subject. He often remarked that one learned more from a single well developed case report than from a long paper on the subject. He particularly delighted in the programs of the American Ophthalmological Society, which always gave him an opportunity to place on record his own experience with an unusual problem. His reports were concise and direct and were typical of his behavior in the office and the hospital, where he always moved with a minimum of lost motion. For more than thirty years he had advocated some form of corneoscleral suture in cataract extraction and was one of the first in this country to attempt intracapsular extraction except where contraindicated. Extensive travels abroad allowed him to visit outstanding clinics and to observe various ophthalmic surgeons at work, and his practice always received the immediate benefit of such surgical procedures as appealed to him. He could converse passably in French and Spanish, but language barriers never deterred him from obtaining the information he needed. He returned from the International Congress of Ophthalmology in 1929 to apply immediately Gonin's technic in the treatment of retinal detachment. Unable to understand the presentation at the meeting, he had smoothed out all the details with Gonin during a chance meeting on a streetcar the following day.

Persistence and the attention to detail were primary virtues with Dr. Ellett. His office records, written in long hand, were masterly in description, but always brief and to the point. If the diagnosis was obscure, there was no quibbling over terms; treatment was prescribed as seemed indicated and if the course of the disease was not altered in a few days there was no hesitancy in a change to some other form of therapy. There was neither dogmatism nor nihilism in his treatment of his patients, and it was often amazing to mark the improvement of patients with stubborn conditions unyielding to the accepted forms of therapy. His quiet manner and gentle touch always inspired confidence, which is itself a primary requisite in treatment.

He was a man much honored by his colleagues. In 1914 he served as Chairman of the Section on Ophthalmology of the American Medical Association and was president of the American Academy of Ophthalmology and Otolaryngology in 1926 and of the American Ophthalmological Society in 1932. In addition, he held executive positions in all local and sectional medical organizations, having been president of the Memphis and Shelby County Medical Society and of the Tennessee Academy of Ophthalmology and Otolaryngology and vice president of the Southern Medical Association. He was active in the American College of Surgeons and in the Pan-American Congress of Ophthal-

mology and was in constant attendance at sessions of the International Congress of Ophthalmology.

In November 1939 the Southern Medical Association honored him with "Ellett Day," dedicated to a review of his achievements as a physician, citizen and soldier. In October 1942 Dr. Ellett was associate guest of honor of the American Academy of Ophthalmology and Otolaryngology and received the Award of Merit in recognition of his services as president, member of council and instructor, as well as scientist, teacher and soldier. In May 1943 the Memphis and Shelby County Medical Society honored him with a testimonial dinner to celebrate his fiftieth year of medical practice in Memphis, at which were nine Memphis ophthalmologists and otolaryngologists who had been associated with him in private practice during those years.

For many years a member of the board of directors of the National Society for the Prevention of Blindness, and a vice president at his death, he gave freely of his time to the labors of this lay organization in the field of sight conservation. In 1939, in cooperation with the St. Louis Society for the Blind, he was given the Leslie Dana Medal "for outstanding achievements in the prevention of blindness and the conservation of vision."

A member of the original American Board for Ophthalmic Examinations, he helped to conduct the first examinations for certification in ophthalmology at the initial meeting in Memphis, thirty years ago. His interest in this was maintained, and he continued to review candidates' examination papers until last year, when he retired from the American Board of Ophthalmology, after serving as president for several years. This, too, was the occasion of a testimonial by the Board.

During World War I Dr. Ellett served in France as commanding officer of Base Hospital 115, with the rank of lieutenant colonel and received a citation for "exceptionally meritorious and conspicuous service." Discharged as a full colonel in the Medical Corps of the United States Army Reserve, he has been known to all his Memphis colleagues as "The Colonel," a term of honor, endearment and respect, which he accepted modestly.

Dr. Ellett was a member of Calvary Episcopal Church. His fraternal orders were Kappa Sigma and Phi Alpha Sigma. In Memphis, he belonged to the Memphis Country Club, the University Club and the Waponoca Club, which gratified his hobbies of golf, tennis and hunting, pleasures which he enjoyed to the very end of his life.

A keen observer, he maintained a varied interest in local and national affairs of government and in matters of education, both general and professional, and was a devotee of amateur sports. At 60 he began the study of Spanish and received lessons in the improvement of his tennis. His versatility and ability can best be demonstrated by the ease with

which he conducted a family tour of South America when air service was in its infancy and by the excellent game of tennis which he played until he was 72. Golf and hunting he enjoyed until his death.

The success of his professional life may be known from the expression, "Despise not the day of small things," a favorite motto which he followed throughout his daily life. Though his experience was wide and his professional attainments were great, he was always modest and unassuming, willing to listen to the suggestions of others. Indeed, he sought the opinions of his colleagues and not only was delighted to learn from the youngest of them, but always accorded the credit for new ideas to the origin from whence they came. To those of us who were privileged to work with and for him, he was a wise counselor and firm friend, a strong arm on which to rely in times of distress. His interest in his former associates and residents of the Memphis Eye, Ear, Nose and Throat Hospital was constant and unwavering. He aided those he deemed worthy in organized medicine by sponsoring their election to membership in various societies, in reviewing their case reports and theses presented to these societies and in introducing them to the membership when they were accepted. His correspondence with them was of tremendous volume. Regardless of the press of professional duties, he always had time to pen a note to a friend at the end of a hard day's work, and no plea for advice ever went unanswered.

Dr. Ellett was one of the nation's outstanding ophthalmic surgeons. He abhorred the sensational and spectacular, preferring to operate in the safest, simplest way and with a minimum of maneuvers. His manual dexterity, steadiness and surgical judgment were maintained to the very end and were the admiration of all who observed him. Although serious and hard working with respect to his professional duties, "The Colonel" had a divine sense of humor and could always break the tension of a tedious day or a difficult situation with a humorous story or remark which was perfect for the occasion. He had a most retentive memory and could cite references to ophthalmic literature which he had not reviewed for years. It was always amazing to hear him quote remarks from Horace and Tacitus or the obscure poetry of early American authors and statesmen, the result of memory training of sixty years ago.

His great influence will endure, for he was a courteous gentleman, beloved physician and skilled surgeon, a wise counselor and staunch friend.

"And when he fell in whirlwind
He went down as when a lordly cedar green with boughs
Goes down with a great shout upon the hill
And leaves a lonesome place against the sky."

RALPH O. RYCHENER, M.D.

# Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

## Color Sense

A CASE OF ATYPICAL ACHROMATOPSIA. L. L. SLOAN, Am. J. Ophth. **29**:290 (March) 1946.

Sloan reports a case of complete loss of color perception and a shift in the spectral luminosity curve. Her findings indicate that no one of the characteristics commonly associated with typical achromatopsia is invariably present.

W. S. REESE.

## Conjunctiva

PTERYGIUM: ITS NATURE AND A NEW LINE OF TREATMENT. S. KAMEL, Brit. J. Ophth. **30**:549 (Sept) 1946.

In the opinion of Kamel, based on facts deduced from the clinical and pathologic pictures, pterygium is an inflammatory lesion to begin with, while the degenerative changes seen in the deep layers of the conjunctiva are secondary and postinflammatory. Pterygium is an irritative disease. The causes of the irritation are many and various. Two causes are discussed—the influence of locality and the patency of the lacrimal passages. As regards the first, pterygium was common in a village where about 30 per cent of the population were stone cutters, and the condition was common in a second village owing to its location, the inhabitants being exposed to sandy dust which is blown into the village from a strip of sandy desert. The principal step in the operation for pterygium as done by Kamel is dissecting the head of the pterygium from the cornea, undermining the pterygium and conjunctiva up to the canthus and cauterizing the under surface of the conjunctiva with phenol. No stitches are needed.

W. ZENTMAYER.

THE INCIDENCE OF TRACHOMA IN THE SOUTHERN HIGHLANDS PROVINCE OF TANGANYIKA. H. REED, Brit. J. Ophth. **30**:573 (Oct.) 1946.

Trachoma affects about 50 per cent of the Africans of the Bantu tribes in the Southern Highlands Province of Tanganyika. The incidence varies considerably, from 13.7 per cent, in the Rungwe district, to 87.3 per cent, in the neighborhood of Kalenga. Diet, dust, personal habits of cleanliness and the occupation of cattle raising, with the associated swarms of flies, are probably factors affecting the incidence. On the whole the trachoma seen in the Southern Highlands Province is a mild disease.

W. ZENTMAYER.

## Experimental Pathology

CHEMICAL TRANSMISSION OF NERVE STIMULI AND PUPILLARY MOTILITY. R. RODRIGUEZ and W. ISOLA, Arch. de oftal. de Buenos Aires **18**:692 (Dec.) 1943.

The authors have confirmed experimentally the reality of the liberation of sympathin in the aqueous humor by stimulation of the sympathetic pupillomotor nerves, not only by excitation of the cervical sympathetic fibers but by direct stimulation of the hypothalmic center. The experiments were made on dogs. The liberation of sympathin was detected by establishing in vivo a communication of the anterior chamber of the stimulated dog with the anterior chamber of another dog. Excitation of the hypothalamic zone, besides producing bilateral mydriasis in the one dog, caused dilation of the pupil in the other dog. Also, injection of aqueous humor into the heart of a frog produced acceleration. Epinephrine-like substances were detected in the aqueous by the Bayer reaction.

It was observed that during the mydriasis produced by the hypothalamic excitation, direct stimulation of the third nerve had a normal effect on the extraocular muscles but miosis was retarded, and the stimulation had to be prolonged to produce it.

The mydriatic action of the hypothalamic stimulation is transmitted by the fibers of the cervical sympathetic nerve. When these fibers were severed, no mydriasis occurred.

The following conclusions are reached: Sympathin is liberated not only by excitation of the peripheral sympathetic fibers but by stimulation of the hypothalamic centers, the action when central being bilateral; the mydriasis is different from that produced by simple stimulation of the sympathetic fibers; the substances liberated in the aqueous humor in both instances are able to induce motility in the pupil of another animal by humoral action alone.

H. F. CARRASQUILLO.

THE BLOOD-AQUEOUS BARRIER IN HYDROPHTHALMIC RABBITS. J. H. SMITH, Ophthalmologica **108**: 293 (Dec.) 1944.

The University Eye Clinic in Basel, Switzerland, has successfully bred a strain of hydrophthalmic rabbits. In the present experiments, 19 of these rabbits, of different age levels, and 9 normal rabbits were compared as to the time elapsed before the appearance of fluorescein in the anterior chamber after subcutaneous injection. It was found that there was a very considerable delay in the appearance of fluorescein in the hydrophthalmic rabbits as compared with its appearance in the normal rabbits. The weights of the rabbits and the size of the pupil in the two groups were approximately the same. The intraocular pressure in the hydrophthalmic group on an average was about 10 mm. higher than that in the normal group. The author believes that these experiments prove that the rate of flow across the blood-aqueous barrier is definitely and considerably slower in hydrophthalmic rabbits than in the normal rabbits, and this suggests a reduced permeability, probably arising from atrophic conditions produced by the increased intraocular pressure in the eyes of the former.

F. H. ADLER.

## General

OCULAR MANIFESTATIONS OF MALNUTRITION IN RELEASED PRISONERS OF WAR FROM THAILAND. H. RIDLEY, Brit. J. Ophth. **29**: 613 (Dec.) 1945.

The eyes of some 500 released allied prisoners of war and internes from Thailand who considered that their sight had deteriorated during captivity were examined; among these no less than 100 cases of amblyopia were seen in seventeen days. The food had been inadequate in quantity and lacking in variety, being especially deficient in proteins, fats and vitamins. The three daily meals were the same, chiefly polished rice of poor quality. This was supplemented by vegetable stew containing pumpkin, yams, sweet potato, bringal, Chinese radish and Chinese cabbage.

In 90 of the patients, at the time of writing, sight had been defective for two and one-half to three years. Corrected vision varied from 1/60 to a partial 6/9. All those with scotomas and good acuity had recovered from temporary severe amblyopia. In many patients the onset was sudden, maximum disability being reached within a single day. In others it was gradual, taking months to develop. There were few complaints of day blindness. Sight was particularly defective in bright light. Many of the patients with amblyopia had suffered from pellagra, edema of the legs, dry beriberi and such minor lesions as sore tongue and perlèche, which usually accompany deficiency in the B group of vitamins. Quite a number had become nerve deaf. The fundus might show no changes even when the amblyopia was of long standing, though in many there was pallor of the temporal half of the papilla.

Forty-eight patients had optic nerve atrophy, and in 30 more the condition was regarded as doubtful. In a few instances in which temporal pallor was pronounced there appeared to be some constriction of the macular arterioles—a change probably secondary to retinal atrophy.

Ninety patients showed a small, sharply demarcated central scotoma, rarely extending more than 3 degrees, and often 1 degree or less. In the remaining 10 patients the core of the scotoma was paracentral or pericentral. Further details of the nature of the scotoma are given. No defect in the peripheral field was found with rough testing. Practically all the released prisoners showed some degree of keratoconjunctival abnormality. There was no xerosis of the cornea of Bitot's spots. The most striking feature of the limbal capillaries was their variability in size, which was often so great that aneurysms, both fusiform and saccular, were noted. There seems little doubt that the lesions described were due primarily to malnutrition, though other factors may have operated since only a small proportion of men living under the identical conditions were affected. No similar series of cases has occurred in the civilized world until this war. There seems to be no doubt that the diet was deficient generally, especially in proteins, fats and vitamins; in the absence of direct evidence that avitaminosis unsupported by other factors was the cause, it seems advisable to attribute the lesions to general malnutrition rather than to simple deficiency of the vitamin B group.

W. ZENTMAYER.

## General Diseases

OCULAR LESIONS IN SOME SYSTEMIC VIRUS DISEASES. A. SORSBY, Tr. Ophth. Soc. U. Kingdom **64**:67, 1944.

In an opening paper of a discussion on virus diseases of the eye at the annual congress of the Ophthalmological Society of the United Kingdom in 1944, Sorsby enumerates the disease of virus origin in the various structures of the eye as follows:

*Lids.*—Vesicular eruption of herpes zoster ophthalmicus; molluscum contagiosum; common wart

*Conjunctiva.*—Some, at least, of the amicrobial forms of ophthalmia neonatorum; epidemic keratoconjunctivitis; trachoma; Parinaud's syndrome; vaccinia, and pemphigus

*Cornea.*—Superficial lesions: Superficial punctate keratitis; keratitis nummularis; herpes corneae; dendritic ulcer, and herpes zoster. Deep lesions: Disciform keratitis; interstitial keratitis; subepithelial parenchymatous opacities (keratitis parenchymatosa metaherpetica); deep marginal keratitis without ulceration as a complication of influenza, and herpes cornea posterior with recurrent labial herpes.

*Uveal Tract.*—Iritis and iridocyclitis occurring with smallpox, mumps, chickenpox and herpes zoster; choroiditis occurring with smallpox; Harda's disease; sympathetic ophthalmia

*Retina and Optic Nerve and Ocular Muscle.*—Involvement with general virus disease

*Lacrimal Gland.*—Involvement with mumps; uveoparotid fever (possibly) disease.

W. ZENTMAYER.

OPHTHALMOSCOPIC CLASSIFICATIONS OF ARTERIAL HYPERTENSION. C. ESPILDORA-LUQUE, Arch. chilena de oftal. **3**: 5 (Nov.-Dec.) 1944.

After giving the classifications of hypertensive disease based on the retinal lesions, Espildora-Luque expresses the opinion that the one proposed by Gans is the most appropriate. Its simplicity and descriptive expression are unquestionable. He agrees with Gans that the ophthalmologist should adopt a neutral and impartial position. He should describe only his findings in the cases referred to him, leaving to the internist or the surgeon the final decision.

H. F. CARRASQUILLO.

## Glaucoma

DIATHERMIC SURGERY OF THE CILIARY BODY IN GLAUCOMA. M. U. TRONCOSO, Am. J. Ophth. **29**:269 (March) 1946.

Troncoso reviews the thermic methods of treating glaucoma and attempts to determine the physiologic basis of diathermic methods, their action on intraocular pressure and the damage done to the ocular structures. He used rabbits for these experiments but found that the reduction in tension was not permanent. Therefore he considers the results disappointing.

W. S. REESE.

FURTHER STUDIES ON THE USE OF FURMETHIDE IN THE TREATMENT OF GLAUCOMA. E. U. OWENS and A. C. WOODS, Am. J. Ophth. **29:** 447 (April) 1946.

Owens and Woods conclude that furmethide (furfuryl trimethyl ammonium iodide) is a valuable drug in the treatment of glaucoma, especially the severer forms, a 10 per cent solution being more effective than 20 per cent mecholyl chloride and 5 per cent neostigmine methyl sulfate in cases of late primary glaucoma and in those cases of primary glaucoma in which the previous use of other miotics has failed. Systemic reactions are rare, and no evidence of local sensitivity or irritation has been noted.

W. S. REESE.

GLAUCOMA AND CHOKED DISK. L. ECTORS and C. BIGAUX-VAN BOVEN, Ophthalmologica **108:**113 (Sept.) 1944.

The authors give the various factors responsible for the production of choked disk as follows: (1) increase of the cerebrospinal fluid pressure, (2) increase of the intracranial venous pressure, (3) increase of the general arterial blood pressure and (4) decrease of the intraocular pressure. In the cases reported a choked disk due to increased cerebrospinal fluid pressure disappeared as the intraocular pressure became elevated.

F. H. ADLER.

## Hygiene, Sociology, Education and History

OPHTHALMIC PROBLEMS AND VISUAL STANDARDS IN INDUSTRY. J. MINTON, Brit. J. Ophth. **30:**298 (May) 1946.

The following grades of vision are suggested in allocating applicants for employment, whether juvenile or not, to various occupations.

Grade 1. To this group belong all persons possessing 6/6 or 6/9 vision in each eye and also those having 6/6 vision in one eye and not less than 6/36 vision in the other eye. Persons in this group are fit for all occupations.

Grade 2. Persons having visual acuity of not less than 6/12 in each eye and also those having 6/12 vision in one eye and not less than 6/36 vision in the other eye. Working people with grade 2 vision are fit for all industrial occupations except for the very close work essential in the manufacture and inspection, for example, of radio valves and electric lamps, in certain silk yarns trades and in a few others. Grade 2 vision is sufficient for all clerical work, the engineering industry and the driving of vehicles.

Grade 3. In this group are all the one-eyed persons who have 6/6, 6/9 or 6/12 vision in the good eye and less than 6/36 vision in the other eye, or who have one blind eye. The one-eyed persons with 6/6 in the good eye are fit for all occupations, even for those which require fine, close work. The one-eyed persons who have 6/9 or 6/12 vision can be engaged in most trades and industries. Certain occupations, such as coal mining, and certain operations in the engineering trades, such as hammering, chipping, turning and milling, present a greater danger of injury to the eyes. It is therefore suggested that one-eyed workers should not be engaged in coal mining or in any of the aforementioned engineering operations.

Grade 4. To this group belong the working people who have 6/24 vision in each eye, or who have 6/24 in one eye and 6/36 in the other eye. People with grade 4 vision can be employed in all outdoor occupations, building trades, carpentry, dock labor, portering and many similar trades.

Grade 5. To this group belong the blind and partially blind and can include all persons with less than 6/36 vision in either eye. It is pointed out that many young men with a latent hyperopia of 2 or 3 D. have 6/6 vision without glasses on entering the railway service, as required, but at the age of 40 the latent hyperopia becomes manifest and vision drops to 6/18. When the man is reexamined at this age, the required 6/6 vision can be attained only with glasses, and promotion is refused.

W. ZENTMAYER.

ARABIAN OPHTHALMOLOGY. W. B. I. POLLOCK, Brit. J. Ophth. **30:** 445 (Aug.) 1946.

This paper on the Arab school of ophthalmology was read in the summer series of lectures in the department of ophthalmology, University of Glasgow. It does not lend itself to abstraction. Pollock states, however, that it may be said that the Arabic books on ophthalmology were mainly taken from the Greek; but Hirschberg points out that the Greeks had no good ophthalmologic textbook except that of Alexandros, and he was never mentioned by the Arabians. What they took from the Greeks they had to select according to their own plan. They treated the Greek text with the greatest respect, discussed every word and then added their own observations; and they were often accurate in symptomatology, diagnosis and treatment.

W. ZENTMAYER.

## Injuries

SUPERFICIAL "BURNS" OF SKIN AND EYES FROM SCATTERED CATHODE RAYS. L. L. ROBBINS, J. C. AUB, O. COPE, D. G. COGAN, J. L. LANGOHR, R. W. CLOUD and O. E. MERRILL, Radiology **46:** 1 (Jan.) 1946.

Robbins and his associates report injuries received by 6 men in the department of radiology at the Massachusetts General Hospital as a result of a few seconds' exposure to scattered electrons from a 1,200 kilovolt electrostatic generator. The exact dosage could not be determined but was probably between 1,000 and 2,000 "tissue roentgens." The lesions had the unusual characteristic of appearing in three phases, the last one becoming manifest approximately four weeks after the exposure; except for a mild injection of the conjunctiva in 3 men, coming on within a few hours after the exposure, no ocular signs occurred during the first two phases of reaction. Severe ocular signs developed in 1 man in the tertiary phase and consisted of punctate epithelial lesions, accompanied with severe photophobia, lacrimation and a foreign body sensation. Cutaneous lesions elsewhere were present.

J. A. M. A. (W. ZENTMAYER).

ELECTRIC OPHTHALMIA. L. K. WOODWARD JR., U. S. Nav. M. Bull. **46**:247 (Feb.) 1946.

Woodward observed 47 patients with flash burn of the eyes, or electric ophthalmia, on a repair ship. The greater number were men working in the immediate vicinity of the welders, and all these men had momentarily removed their goggles at the time an arc was struck or did not use goggles while at work. The symptoms were principally mild to severe injection of the conjunctiva and, more especially, an episcleral injection. Five men had considerable edema of the eyelids. In 6 men there was evidence of pseudopterygium with accompanying injection. Superficial ulceration of the cornea was present in 2 men. Treatment consisted in irrigation of the eye with mild boric acid solution and instillation of a solution containing tetracaine hydrochloride and neo-synephrine hydrochloride. In many instances an ointment containing 2 per cent butacaine sulfate also was employed. Relief was obtained, especially when there was edema of the lids, by application of cool boric acid compresses. The response to therapy was prompt. About one third of the patients were removed from duty for a period of twenty-four hours.

J. A. M. A. (W. ZENTMAYER).

## Operations

IRIDENCLEISIS—A MODIFICATION. D. P. SMITH, Brit. J. Ophth. **30**: 589 (Oct.) 1946.

The method Smith adopts in performing iridencleisis is described. The pressure of the vitreous is first lowered by a scleral puncture made with a Graefe knife 45 degrees to the temporal side of the vertical meridian and 6 mm. from the limbus. On entering the sclera with a narrow, parallel-sided keratome, an incision is made similar to that for a preliminary iridectomy. With an iris hook the iris is drawn into one angle of the wound and snipped off. By stroking the wound from the opposite end, one pillar of the loop is freed, so that it slips back into the anterior chamber, leaving the other incarcerated. A scissors cut is then made in the conjunctiva 5 mm. above and parallel to (and rather longer than) the keratome incision. The conjunctiva is then undermined with two pairs of fine forceps, and the lips of the conjunctiva over the keratome incision are then pinched together; they adhere because the elastic pull has been abolished by the conjunctival incision. This wound serves the added purpose of providing a temporary outlet for the aqueous, so that the lower conjunctival wound is not forced open again but has time to unite. The article is illustrated.

W. ZENTMAYER.

## Orbit, Eyeball and Accessory Sinuses

THE SCLERAL-RESECTION (EYEBALL-SHORTENING) OPERATION. D. VAIL, Am. J. Ophth. **29**:785 (July) 1946.

Vail opens this de Schweinitz Lecture with praise for the work done by de Schweinitz as a medical officer during World War I. He then reviews the history, technic and case records of scleral resection and reports a case of bilateral scleral equatorial staphyloma and detached retina cured by scleral resection.

W. S. REESE.

PROPTOSIS—DIFFERENTIAL DIAGNOSIS. F. MASSOUD, Brit. J. Ophth. 30:622 (Oct.) 1946.

It is not possible to make a satisfactory abstract of an article of this nature. Massoud gives the following summary of the classification of proptosis employed and the conditions which may be encountered in each category.

*Apparent.*—Globe not displaced; high myopia; buphthalmos; megalophthalmos; staphyloma; paralysis of the seventh nerve.

*Due to Congenital Anomaly.*—Arrested development; premature ossification; shallow orbit; cranial hernias appearing as tumor masses; vascular, nervous, mixed.

*Due to Traumatic Injury.*—Intracranial—tear of internal carotid artery or cavernous sinus; intraorbital—aneurysm of the ophthalmic artery; extraorbital—tear of carotid artery or jugular vein; late effect—proliferation.

*Due to Inflammatory Process.*—Acute—from injury or extension, abscess, cellulitis, thrombophlebitis, anthrax; subacute—mucocele, retrobulbar, subperiosteal; chronic—tuberculous, syphilitic, actinomycotic, hyatid, etc.; late effect—from obstruction.

*Due to New Growth.*—Intracranial—meningioma, osteoma; oral and nasopharyngeal—myxoma, chondroma, plasmoma, osteoma; orbital—cavernous angioma, osteoma, lacrimal cylindroma, carcinoma; ocular—from optic nerve and sheath, choroid, retina; metastatic—sarcoma, carcinoma.

*Due to Systemic Condition.*—Sympathetic—exophthalmic goiter; endocrinal disturbance—malignant exophthalmos; metabolic—scurvy, rickets, hemophilia; hyperplastic—leukemias, xanthomatosis, Paget's disease (osteitis deformans).

Methods of diagnosis include general examination, history taking, transillumination; roentgenographic examinations; tests and cytologic studies of the blood, special laboratory tests; medical and surgical procedures.

W. ZENTMAYER.

## Pharmacology

A CLINICAL TRIAL OF A SYNTHETIC MYDRIATIC (DIMETHYLAMINOETHYL BENZYLATE ETHOCHLORIDE [BENZILYLOXYETHYL DI-METHYLETHYL AMMONIUM CHLORIDE]). W. J. B. RIDDELL, Brit. J. Ophth. 30:1 (Jan.) 1946.

This substance (benzilyloxyethyl di-methylethyl ammonium chloride), referred to as E3, in 1 per cent aqueous solution was compared with a 1 per cent solution of atropine sulfate and a solution of 1 per cent homatropine hydrobromide and 2 per cent cocaine. The impression was obtained that the new substance is probably an efficient substitute for homatropine both as a mydriatic and as a cycloplegic.

The action of E.3 in 1 per cent solution is neither so rapid nor so prolonged as that of atropine. It reaches a maximum in an hour, and the effect commences to fall off in five or six hours. No cutaneous irritation was found in subjects known to have sensitivity. No changes were observed in the corneal epithelium.

W. ZENTMAYER.

A NEW SYNTHETIC MYDRIATIC. I. MANN, Brit. J. Ophth. **30**:8 (Jan.) 1946.

Mann found that the synthetic mydriatic known as E.3 (benzilyloxyethyl di-methylethyl ammonium chloride) can be used for diagnostic and refractive purposes in the same way as atropine. Its action is more easily reversed by physostigmine than is that of atropine, but in old people it is not so safe as is homatropine. It appears to lie between atropine and homatropine in its strength of action on normal eyes. None of the patients made any complaint of discomfort from its use.

This synthetic mydriatic is nonirritating and nontoxic. It is in all respects suitable as a substitute for atropine, though it may have to be used more frequently.

W. ZENTMAYER.

## Refraction and Accommodation

THE EFFECT OF SUNLIGHT ON DARK ADAPTATION. B. CLARK, M. L. JOHNSON and R. E. DREHER, Am. J. Ophth. **29**:828 (July) 1946.

The authors found that persons exposed to sunlight for three to four hours a day over a period of two weeks showed a marked elevation of the night visual threshold immediately after exposure. The degree of elevation persisting overnight is sufficient to cause approximately a 50 per cent loss in night visual efficiency. These effects are temporary.

W. S. REESE.

UNAIDED VISUAL ACUITIES CORRELATED WITH REFRACTIVE ERRORS. M. H. PINCUS, Am. J. Ophth. **29**:853 (July) 1946.

The physical examination records of 45,206 men and women as well as 7,482 refraction records were reviewed for this study, which was designed to correlate the unaided visual acuity with the different refractive errors. It was undertaken to supply the need of a simple method to detect malingerers.

W. S. REESE.

## Retina and Optic Nerve

RADON SEEDS IN THE TREATMENT OF GLIOMA RETINAE. S. PHILPS, Tr. Ophth. Soc. U. Kingdom **64**:107, 1944.

A boy 5 months old had the left eye removed for glioma of the retina. The right eye was normal. Four and one-half years later a glioma was noted in the upper nasal quadrant of the right eye. Permission for removal of the eye was refused by the parents, as an older brother had bilateral enucleation for glioma of the retina and died of intracranial extension. A 3 millicurie radon seed was inserted in the growth and removed ten days later. The growth "shrank away." On two subsequent occasions reapplication of radon seeds was made for what was thought to be recurrence of the growth at the site of the original tumor. Three years later the eye was free from growth and visual acuity equaled 6/12. There were macular changes resembling retinitis circinata. At the age of 19 vision was somewhat reduced, owing to irradiation cataract. The author believes that what was supposed to be recurrence was in fact reparative fibrous tissue and that therefore the subsequent irradiations

were unnecessary. In the second case the diagnosis was that of bilateral glioma retinae in a boy aged 8 months. The left eye was almost full of growth and was removed. In the right eye the growth was globular and measured 6 disk diameters in each direction. A 2.5 millicurie radon seed was introduced into the center of the growth. At the time of the report, three years and four months after irradiation, all that remained of the growth was a small, mulberry-like nodule, which had remained unchanged for two years. It seems unlikely that there remained any active growth in the eye. Visual acuity was about 6/12.

W. ZENTMAYER.

THE OPTIC NERVE AND THE MESSAGES IT TRANSMITS. A. MAGITOT, Ann. d'ocul. **179:** 24 (Jan.) 1946.

The introduction to this article deals with a brief anatomic description of the optic nerve and how it differs from other sensory nerves in various ways, such as in not having a sheath of Schwann. This is followed by a general discussion of the physiologic properties concerned with the transmission of impulses in sensory nerves. The author discusses such topics as summation, the all or none law, amplitude and the latent period. The research work on the chronaxia in man and animals is reviewed.

The objective measurement of the visual response is fully covered, especially the work of Hartline and Granit. Hartline's work on single nerve fibers in the frog retina, in which it is shown that three types of fibers are present, and Granit's work on color vision are applied to present day concepts of vision. The author feels that from anatomic and physiologic studies one must admit that the optic nerve contains both visual and pupillomotor fibers.

In conclusion, an attempt is made to correlate the clinical findings in diseases of the optic nerve with the physiologic knowledge of its function. As an example, the author cites the controversy concerning the site of intoxication in tobacco amblyopia. In this condition the chronaxia is normal, placing the lesion in the visual cells, the rods or cones (with involvement of the bipolar cells the chronaxia has been shown to be abnormal). Because the centrocecal scotoma is for red, the lesion can be still more accurately localized in those cones that Granit considers to be concerned with the appreciation of red.

This article should be read in full by those interested in the physiology of vision.

P. R. MCDONALD.

EXUDATIVE RETINITIS OF COATS: REPORT OF A CASE. J. P. JOLY, Arch. d'opht. **6:** 46, 1946.

A youth aged 19 had a complete cure of exudative retinitis, occurring either spontaneously or as the result of intravenous injections of salicylates. The patient had all the classic signs of the disease described by Coats in 1908. His general health was perfect; tuberculosis could not be demonstrated. There was coexisting cyclitis. The case is presented because of the relatively favorable outcome in a condition for which the prognosis is usually bad.

S. B. MARLOW.

RETINAL CYSTS. O. KURZ, Ophthalmologica **107:** 233 (May-June) 1944.

The author divides retinal cysts into two types: (1) those associated with a retinal detachment, and (2) those with no associated detachment. This differentiation is based on the ordinary ophthalmoscopic examination, but the author points out that in some cases a detachment of the macular region may be present which can be detected only by means of examination of the fundus with the slit lamp (the author used the Goldmann apparatus for this purpose).

Two cases are described in which cysts occurred with a characteristic picture of detachment below and tears in the ora serrata. Cysts of this type occur frequently in the eyes of youthful (not myopic) patients. The detachment is usually in the lower temporal portion of the retina, shows little tendency to progression and exhibits an inclination to spontaneous delimitation through the formation of a choroidal barrier. The disease is frequently latent for a long period, without the patient's knowledge. The operative prognosis is generally favorable.

The condition frequently occurs symmetrically in the two eyes and occasionally is familial. Two cases of this type are described, and the pathogenesis of cyst formation is discussed. Two other cases of uncomplicated cyst formation are reported. The diagnoses in these cases were idiopathic cyst and cyst following choroiditis. Their pathogenesis is also discussed.

F. H. ADLER.

SYMPTOM COMPLEX OF CHORIORETINITIS CENTRALIS SEROSA (KITAHARA). R. BRÜCKNER and N. H. FIELD, Ophthalmologica **109:** 281 (June) 1945.

Three cases of this disease are reported. The characteristic signs are described.

1. Ophthalmoscopic Findings. There is a flat detachment in the macula, which is made evident by a sharply limited ringlike reflex. At the beginning this area may be somewhat deeper colored than normal. The area affected is usually circular, but it may be elliptic. After three to five weeks' duration, numerous small yellowish points appear within this area, and after healing only a few lightly pigmented spots may remain.

2. Subjective Symptoms. These consist of a relative, more or less intensive, positive scotoma, together with alterations in the color sense. Occasionally, micropsia and metamorphopsia may be present, but the lowering of the visual acuity is usually slight. In general, the visual acuity returns to normal, even after a duration of several months. In some cases the hyperopia undergoes a transitory increase.

3. Recurrences. These are frequent. Kitahara reported cases in which there were fourteen recurrences over a period of three years. As a rule, the recurrences affect the same part of the retina. The author believes that the primary changes are localized in the choroid and may be the result of a nonbacterial allergic reaction. He suggests that the tubercle bacillus may play a role. He also considers the possibility that the disease is a vascular disturbance of nervous origin. He points out the difficulties in making the diagnosis early and suggests that the following technics, if employed, will enable one to make

a diagnosis earlier than usual: 1. Focal illumination of the fundus. 2. Entopic proof of a positive scotoma by illumination through the sclera (which he refers to as "disscleral transillumination"). This succeeds in eliciting a scotoma when the patient is not spontaneously aware of it. 3. Entopic proof of the detachment of the retina by disscleral illumination.

The article contains a very good colored plate of the eyegrounds.

F. H. ADLER.

THE RELATION OF PERIPHLEBITIS RETINAE AND RECURRENT JUVENILE VITREOUS HEMORRHAGES TO THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE). A. E. SCHMID, Ophthalmologica **110**: 259 (Nov.-Dec.) 1945.

Eighty-six patients with thromboangiitis obliterans and 25 patients who had periphlebitis retinae and recurrent hemorrhages in the vitreous were examined in order to determine whether there was any relationship between these two conditions, as claimed by Marchesani (*Arch. f. Augenh.* **109**: 124, 1935). Schmid could find no proof that these two conditions are in any way related. He believes that periphlebitis retinae is due almost exclusively to tuberculosis.

F. H. ADLER.

## Tumors

IMPORTANCE OF EXAMINATION OF THE NERVE SHEATH IN CASES OF TUMOR OF THE OPTIC NERVE. MONBRUN, G. OFFRET and J. GUILLAUME, Arch. d'opht. **5**: 8, 1945.

The authors point out that in histologic descriptions of tumors of the optic nerve the sheath is often passed over without notice or is insufficiently examined. They described a case in which operation was performed in 1937 and present a histologic study with photomicrographs of the tumor. In the nerve sheath proliferation of the glial tissue was evident. A second, much more complex, case was described. The authors review some of the reports in the literature. They try to show, first, that certain unexplained facts about tumors of the optic nerve become clear when gliosis or gliomatosis of the perineurium is considered. Second, the data which they have accumulated favor the idea of a congenital dysplasia in certain of these tumors. As the result of their histologic studies, they believe that when a tumor of the optic nerve is examined the whole sheath should be carefully studied.

S. B. MARLOW.

ANGIOMAS OF THE ORBIT. G. RENARD and G. OFFRET, Arch. d'opht. **6**: 284, 1946.

This is an anatomic and pathologic study of angiomas of the orbit. Anatomic cavernous angioma is the most frequent form. It is a circumscribed condition and not infrequently occurs within the muscle cone. A number of cases are presented, with histologic drawings, and an extensive histologic study is reported. In addition to the cavernous angioma, angioma lipoma and hemolymphatic angioma are discussed. In conclusion the authors state that care must be exercised in the classification of angiomas of the orbit. As a matter of fact, only a

small number of them have been accurately classified. It is not necessary to introduce a new terminology. A bibliography is appended.

S. B. MARLOW.

PLASMOMA OF THE CONJUNCTIVA. H. CORTES, Arch. Soc. oftal. hispano-am. **4:** 238 (April) 1945.

A woman aged 21 presented partial ptosis of the right upper lid. The skin of the lid was raised, and there was ectropion of the inner two thirds. The exposed conjunctiva showed a fleshy mass with vegetations of a pink color. On eversion of the lid, a large, fleshy, papillomatous mass was observed. The mass was divided in three formations by deep folds. Its color resembled somewhat that of vernal conjunctivitis. The lower lid presented folliculosis. There were no subjective symptoms. The left eye was normal.

Histopathologic examination showed that the mass was chiefly formed of newly formed tissue rich in plasmocytes with many lymphocytes and polymorphonuclear leukocytes in nodular formations. The diagnosis of trachoma was ruled out. The tumor was treated by excision with the diathermy loop.

The article contains numerous photographs and photomicrographs.

H. F. CARRASQUILLO.

A CASE OF EPITHELIOMA OF THE LACRIMAL GLAND. A. MOREU and E. FORNES, Arch. Soc. oftal. hispano-am. **6:** 59 (Jan.) 1946.

A case of epithelioma of the lacrimal gland is reported. The tumor is extremely rare. A woman aged 46 gave a history of her trouble having begun when she was 16 years of age. Very insiduously the right eye began to proptose and diplopia developed. At the time of examination she presented a hard, freely movable, bilobulated mass in the region of the lacrimal gland. There was paralysis of the sixth nerve. Operation was performed for a benign neoplasm of the gland, but histologic examination revealed an epithelioma. Photomicrographs are shown.

H. F. CARRASQUILLO.

NEUROMA OF THE OPTIC NERVE AFTER ENUCLEATION. JEAN BABEL and MARIO VALERIO, Ophthalmologica **109:** 317 (June) 1945.

A man aged 40 received an injury to his left eye which necessitated its enucleation. After this persistent neuralgia developed in the left orbit, followed by a chronic inflammatory process. Surgical exploration of the orbit revealed an amputation neuroma, accompanied with a chronic inflammatory cellular infiltration. In the adherent stump of the optic nerve there was a small granuloma with giant cells. The authors believe that the neuroma originated in the ciliary nerves.

F. H. ADLER.

## Uvea

SEROUS CENTRAL CHOROIDITIS. P. BONNET, L. PAUFIQUE and BONAMOUR, Arch. d'opht. **6:** 129, 1946.

The authors point out that this condition is not well known in Europe but has received especial attention in Japanese literature. The

bibliography is rich in articles under many titles, all of which probably designate cases of this disease. The authors describe the clinical picture, which begins with loss of vision and color scotomas. In the early stages vision may be improved with a convex spherical lens. The ophthalmoscopic picture is described in detail. The macula is the site of a bullous swelling, sometimes red and sometimes orange, with surrounding brilliant reflexes. This swelling may have an elevation of 3 or 4 D. or more, and its walls are sometimes rather transparent. In the presence of such a large lesion the visual disturbance is extreme. The condition usually becomes bilateral sooner or later. There are cases of the extramacular form of the disease. In the differential diagnosis cysticercosis must be taken into consideration. The cause is not definitely known, although there is evidence that tuberculosis is an important factor. The authors have never found that syphilis was the cause. They report observations on 7 cases, with drawings and photographs.

S. B. MARLOW.

TWO CASES OF UVEITIS ASSOCIATED WITH ALOPECIA, VITILIGO, DYSACUSIA AND POLIOSIS (VOGT-KOYANAGI SYNDROME). S. BARRENECHEA and R. CONTARDO, Arch. chilena de oftal. 2:5 (Sept.-Oct.) 1944.

Two cases of the Vogt-Koyanagi syndrome are reported in women aged 44 and 26, respectively. In the first case vision was reduced to counting of fingers and perception of hand movements and in the other to perception of light. In 1 case all the cardinal symptoms of the condition were present, and in the other only dysacusia was missing. Both patients had evidences of infectious processes at the apex of the teeth. They were treated similarly by extraction of the diseased teeth and with vitamins (vitamin B complex, ascorbic acid, nicotinic acid).

The ultimate results of the treatment were as follows: In the first case vision after eleven months was limited to counting fingers at 1 meter in the right eye and was 2/10 in the left eye. In the second case, in which complicated cataracts were extracted, vision after two years was 4/10 in each eye.

H. F. CARRASQUILLO.

## Vision

PROBLEM OF NIGHT VISION. K. KEKCHEYEV, Am. Rev. Soviet Med. 1:300 (April) 1944.

Kekcheyev points out that methods developed in prewar days for changing visual thresholds by application of caffeine or strychnine had been of laboratory interest only. The literature offered a few suggestions for altering the threshold of certain sensory organs by stimulating other sensory organs. It was established that the stimulation of any external sensory organ (hearing, smell, touch and taste) may augment or diminish the thresholds of visual perception. The author showed that a change in the acuity of night vision produced by stimulation of other sensory organs was not an isolated process but was part of a diffuse autonomic reflex. The thresholds of night vision varied with the pulse rate, the blood pressure level, respiration and electrical resistance of the skin to direct current. Not all stimuli were equally effective in raising the threshold

of night vision. Taste, cold and proprioceptive (moderate effort) stimuli were chosen as being the most practical and convenient. During drowsiness the sensitivity of the eye shows a sharp decrease. The application of cold not only restores vision and hearing but terminates drowsiness as well. By application of taste, cold and proprioceptive stimuli the period of dark adaptation was reduced to from five to six minutes. The acceleration of the dark adaptation period is of great practical importance under battle conditions—for instance, for night fliers, who must discern the enemy bomber in the gloom of the night, in so-called dazzling of the eyes by a searchlight, rocket or the flash of tracer bullets. Experiments carried out in 1943 in the author's laboratory in Moscow showed that the use of red eyeglasses five to ten minutes after the white light has begun to act promptly restored vision to its normal threshold and occasionally intensified it. Thus, the same white light which had previously destroyed the sensitivity of the dark-adapted eye increased that sensitivity when filtered through red glasses. J. A. M. A. (W. ZENTMAYER).

RELATIONSHIP OF VISUAL ACUITY TO THRESHOLD OF BRIGHTNESS PERCEPTION. J. TEN DOESSCHATE, Ophthalmologica **108: 187** (Oct.-Nov.) 1944.

If two stimuli affect a sense organ with intensities $B$ and $B'$, respectively, the subject will be able to discriminate between the two if the difference is above the threshold level. This threshold level is known as $\Delta B$. In the present series of experiments, in comparing two brightnesses, $B$ and $B'$, the threshold, $\Delta B$, is determined under such conditions that the brightness $B$ fills the whole visual field, while brightness $B'$ is observed in a circular test field at a visual angle, $g$, with foveal fixation. Under these conditions, the author has examined the manner in which $\frac{B}{\Delta B}$ depends on (1) the brightness of $B$; (2) the visual angle, $g$, and (3) the state of adaptation of the eye. The results of these experiments are discussed and compared with those of other investigators. It was shown that the visual acuity, $B$, and $\frac{B}{\Delta B}$ depend in an identical way on the brightness. The results of these experiments are in accordance with the recent calculations of de Vreis (*Physica* **10:** 553, 1943), which take into account the statistical fluctuations in the number of light quanta which are "hitting" the various retinal regions.

F. H. ADLER.

## Vitreous

SACCULAR PROLAPSE OF THE VITREOUS BODY. R. A. POIRIER, Am. J. Ophth. **29:**845 (July) 1946.

Poirier reports the case of a white man who had an injury of the right eye in 1918, with later development of a dislocated lens. The eye was divergent and the lens partly absorbed, and there was saccular herniation of the vitreous through the pupil. Because of increased tension, capsular remnants were removed through a keratome incision, accompanied with loss of vitreous. Recovery was uneventful, and vision of 6/7 was obtained with lenses.

W. S. REESE.

INTRAVITREAL INJECTION OF PENICILLIN IN A CASE OF INCIPIENT ABSCESS OF THE VITREOUS, FOLLOWING AN EXTRACAPSULAR CATARACT EXTRACTION. A. FEIGENBAUM and W. KORNBLÜTH, Ophthalmologica **110**:300 (Nov.-Dec.) 1945.

A case of an abscess in the vitreous following extracapsular cataract extraction and its complete cure by intravitreal injection of penicillin is described. The adjuvant value of subconjunctival injections in overcoming the infective process is stressed. The probability of synergistic action from the simultaneous use of sulfadiazine is mentioned.

F. H. ADLER.

## Therapeutics

CONTROL OF EXPERIMENTAL ANTERIOR-CHAMBER INFECTIONS WITH SYSTEMIC PENICILLIN THERAPY. A. E. TOWN, F. C. FRISBEE and J. G. WISDA, Am. J. Ophth. **29**:341 (March) 1946.

Town, Frisbee and Wisda were able to control experimental infections of the anterior chamber of rabbits with massive doses of penicillin given intramuscularly, and in the absence of injury to the lens normal function of the eye was restored.

W. S. REESE.

THE INTRAOCULAR USE OF PENICILLIN. I. MANN, Brit. J. Ophth. **30**: 134 (March) 1946.

The subject is discussed under two headings: experiments on rabbits and the use of penicillin intraocularly in man.

The result of the injection of various solutions of penicillin into the anterior chamber is to produce a reactive aseptic anterior uveitis of varying severity. Even 100 per cent pure penicillin produces some reaction. When the solution was injected into the vitreous, the immediate effect was the formation of a localized opacity in the vitreous, with the track of the needle leading up to it. From the fifth to the seventh day a severe retinochoroiditis accompanied by various vascular changes occurred; at the same time the nerve head became swollen, and in most cases there was the suggestion of thrombosis of the central vein. The pathologic observations at the end of two months in a case of a severe reaction are given. The condition would seem to be a most complete neuroretinal degeneration, followed by fibrosis and accompanied by thickening and fibrosis of the choroid. In all the eyes tested with pure penicillin the course of the events was much milder and none of the eyes became blind.

It appears, therefore, that the serious results obtained with the impure samples were due not to the penicillin itself but to something else, unidentified, which produced the intense pathologic change. In order to decide whether intraocular injection of penicillin was likely to be of therapeutic value, an endeavor was made to find out how long it remained in the eye after one or two injections into the anterior chamber. It would appear that strong inhibitory action can be expected for at least six hours but that persistence for much longer is unlikely. No evidence was found that an aqueous altered in constitution would retain penicillin longer.

The clinical notes in cases of perforating injuries of the eyeball and a case of corneal ulcer with hypopyon in which penicillin was used in the anterior chamber are given.

It would appear that intraocular injection of high concentrations of penicillin is justifiable in severely injured or infected eyes but that the best results are to be expected when the infection is confined to the anterior segment of the eye and the penicillin does not come in contact with the vitreous. Further work with purer solutions might give better results in these cases.

W. ZENTMAYER.

PENICILLIN IN OPHTHALMOLOGY: THE BACTERIOLOGICAL, EXPERIMENTAL, AND CLINICAL EVIDENCE OF ITS VALUE, INCLUDING A PERSONAL SERIES OF 125 CLINICAL CASES. C. A. BROWN, Brit. J. Ophth. **30**:146 (March) 1946.

Brown reviews the literature on the bacteriologic, experimental and clinical evidence of the value of penicillin in ophthalmology and reports on his experience with treatment in 125 clinical cases. Penicillin is established as the most effective therapeutic agent for acute mucopurulent conjunctivitis, as of real value in the treatment of acute keratoconjunctivitis and of great value in preventing secondary infections by early application after injury and, if infection has supervened, in sterilizing the conjunctival sac while the injured tissues recover. The value of penicillin with traumatic infection of the anterior segment is not yet established, but if an obviously septic wound is present it is definitely indicated. Penicillin is of value in the treatment of deep infections of the eye of bacterial origin. Three cases of sensitization to penicillin are described.

W. ZENTMAYER.

LOCAL TREATMENT OF INTRABULBAR INFECTIONS: 6. TREATMENT OF STAPHYLOCOCCUS PANOPHTHALMIA BY INTRABULBAR INJECTION OF PENICILLIN. G. ROENNE, Brit. J. Ophth. **30**:405 (July) 1946.

For the present it is justifiable to assume that in penicillin ophthalmologists possess the best weapon so far at their disposal for combating intraocular infections and that local treatment offers a number of advantages not possible with general treatment, viz.: (1) a bactericidal concentration of penicillin is maintained for a long period, sixteen to twenty-four hours; (2) only small quantities of penicillin are necessary, and (3) as Leopold and Struble and Bellows have shown, general treatment with penicillin does not lead to any demonstrable concentration in the vitreous, or at any rate in only very small quantities. Roenne draws the following conclusions: 1. In therapeutic concentrations of 100 to 500 Oxford units the injection of penicillin into the vitreous body is practically harmless. 2. Intravitreal treatment of infections of the vitreous body with penicillin is extraordinarily effective as compared with other forms of application and other substances. 3. The effectivity of the treatment is directly proportional to the concentration of penicillin. 4. Within fairly wide limits the results of the treatment are dependent only on the number of bacteria in the eye, and not on the interval between inoculation and treatment. 5. The method employed provides indirect information as to the velocity of the absorption of the penicillin from the vitreous body.

The values found agree very well with the results gained by direct bioanalysis. 6. The velocity of the absorption of penicillin from the vitreous body is expressed by the halving time, about six hours. 7. The function log bacteria concentration–log therapeutic penicillin concentration is of first degree. 8. For intrabulbar, especially intravitreal, inflammation, the injection of penicillin into the vitreous body is the best therapy at the moment.

W. ZENTMAYER.

PENICILLIN IN TREATMENT OF COMMON EXTERNAL EYE INFECTIONS. JOSEPH MINTON, Brit. M. J. **2**: 324 (Sept. 7) 1946.

The author found that in treatment of external ocular infections in children penicillin was of advantage in blepharitis and conjunctivitis. The drug was used in the form of an ointment with the former and in the form of drops, 1,000 or 2,000 units per cubic centimeter, with the latter. In treatment of external infections in adults satisfactory results were obtained with the same remedy. The drops were used four times a day, and the infections cleared up rapidly. If a corneal ulceration was present, the same treatment was given combined with atropine and hot compresses. Dendritic ulcers were not benefited and were treated with 30 per cent drops of sulfacetimide, atropine and hot compresses. In a number of adults, after use of penicillin in the form of drops or ointment, the skin of the lids became red and edematous, and the reaction often extended to the skin of the cheek and forehead. This reaction was not due to the composition of the ointment but was produced by the penicillin. The author found that the industrial ocular injuries were best treated with drops of a penicillin solution.

The life of a penicillin solution is limited, as penicillin is hydrolyzed in the presence of moisture. The stability of penicillin is also affected by the $p_H$ of the solution. The stability is also influenced by the temperature. Investigation of the actual life of a penicillin solution shows that at room temperature the solution retains between 90 and 100 per cent of the original potency for eight days. On the fourteenth day the potency had fallen to 75 per cent. The $p_H$ of the solution also enters into the question of stability, and it is important that the $p_H$ be as close as possible to that of tears, which is 7.2.

Directions for the preparation of the drops and of the ointment are given in the article.

The deterioration of penicillin in eye drops is much more active at room temperature than when the solution is kept in a refrigerator. As a rule, the useful life of the solution is between two and three weeks.

ARNOLD KNAPP.

USE OF CIBAZOL [SULFATHIAZOLE] IN OPHTHALMOLOGY. E. BÜRKI, A. E. SCHMID and G. SAUBERMANN, Ophthalmologica **106**: 113 (Sept.) 1943.

This paper is a lengthy report on the authors' experience with sulfathiazole in various ophthalmic conditions. They find that the chief indications for this form of treatment are erysipelas of the lids, ophthalmia neonatorum, serpent ulcer, catarrhal ulcer and infiltrates, tuberculosis of the eye, gonococcic iritis and intraocular infection following perforating injuries.

F. H. ADLER.

# Book Reviews

**Medicine in the Changing Order.** Report of the New York Academy of Medicine, Committee on Medicine and the Changing Order. Price, $2. Pp., 240. New York: Commonwealth Fund, 1947.

This little volume represents the work of a group appointed in December 1942 to study the complex problems of adequate medical care. For the purposes of research, collection of information and eventual recommendations, no less than eleven subcommittees were appointed to deal with such subjects as medical education, undergraduate and postgraduate; internships; the hospitals; administration of public health services; industrial and rural medicine; consultant services; nursing, and dentistry. As finally composed, the committee was made up of thirty-three physicians and seventeen lay persons, selected, on the one hand, from the fields of medical education and public health, and, on the other, from the ministry, the law, social welfare, the hospitals, insurance, labor and industry.

Financed by the Commonwealth Fund, the Milbank Memorial Fund and the Josiah Macy Jr. Foundation, the collected reports form an authoritative and instructive body of information on matters of public health; cost and quality of medical care, urban and rural, throughout the nation; preventive medicine, and insurance, both voluntary and compulsory. While the various suggestions and recommendations do not lend themselves readily to summary or logical analysis and critique, they do repay those who will read, mark, and inwardly digest. The present reviewer would call attention particularly to the opening chapters. One deals with the origins of present problems in American medicine before 1800 and a study of the economic, social, political and industrial factors, as well as the factors more strictly concerned with the profession and practice of medicine, including dentistry, nursing, and hospitalization. Another chapter, entitled "Medicine and the Changing Order," carries on the historical survey to recent decades, with a study of the influence of industrialism, the relation of poverty to medical care, the rise of big business and big government, the emergence of social insurance and the health of the nation.

The method and the goal of medical and public health services must be extended, with their organization and quality preserved and/or improved by effective use of adequate hospital facilities, trained professional and nonprofessional personnel and the organization and cooperation of physicians, with their education, as well as that of the public, adapted to the various needs of the community. Government aid will be required. All in all, the book is a noteworthy contribution which reflects great credit on the committee, and as a *Festschrift* comes most appropriately at a time when the parent organization, the New York Academy of Medicine, is about to celebrate its centennial anniversary —one hundred years of helpful activity in so many matters pertaining to the health of the community.

PERCY FRIDENBERG, M.D.

**Archivos de la Asociacioń para evitar la Ceguera en Mexico (Archives of the Association of Prevention of Blindness in Mexico).** Director, Dr. Luis Sánchez Bulnes; Chief Editor, Dr. Daniel Silva. Vol. IV. Pp. 605. México, D.F.: Secretariá de educación publica, 1946.

The book brings a report of the work done in the hospital of the association in México, D.F., during 1946 and a description of the activities in the various departments. A variety of pictures represent the tragedy of blindness as conceived by various Mexican artists who participated in a contest held by the association on "Art and Ophthalmology."

There are, in addition, thirty-five interesting articles on ophthalmic subjects by local and American authors, of which the following two are summarized:

1. Ophthalmologic Investigation in the Zone of Onchocerciasis in Chiapas, Mexico. Drs. M. Puig Solanes, Anselmo Fonte and José Antonio Quiroz. The diagnosis of onchocerciasis was based on the presence of nodules, on the observation of parasites and on biopsies of the skin. Men are more often affected, owing to occupational habits, and the patients are mostly under 40 years of age. Ocular involvement occurs in 75 per cent of cases. The patients complain of burning, photophobia and the sensation of a foreign body in the eyes. A number of patients had entoptic vision of microfilarias. Most of the patients in the group studied had corneal lesions, which in the majority were those of superficial punctate keratitis. With the slit lamp it is possible to see filiform opacities of uniform length, straight or S shaped, which have been interpreted as remnants of the parasites. As a rule the corneal involvement is bilateral and symmetric but impairs vision very little. The involvement of the iris is characterized by a torpid process which involves mainly the posterior structures, giving origin to the classic downward deviation of the pupil and seriously affecting vision. Cases of secondary glaucoma and phthisis bulbi have also been observed.

2. Necessity of Recognition of Biastigmatism" in Fitting of Contact Lenses. Dr. Manuel Márquez. The author states that the existence of biastigmatism is a daily observation, as in most of the cases, after the correction of corneal astigmatism, there is a residual astigmatism. The contact lens corrects only the corneal astigmatism and leaves unaltered the residual astigmatism. The latter is 0.25 D. in most cases, though in some instances it is as high as 2 or 4 D. The author suggests the use of his procedure of subjective ophthalmometry to determine the spherical error and the corneal and residual astigmatisms. The residual astigmatism can be corrected either by incorporation of the correction in the contact lens or with ordinary glasses.

HUMBERTO ESCAPINI, M.D.